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RING CLOSURES IN THE FLUORENE SERIES

BY

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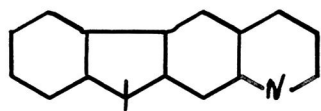
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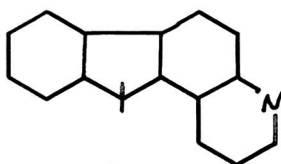
OBJECT OF RESEARCH

Diels, in 1902, (1) studying the monosubstitution derivatives of fluorene applied the Skraup quinoline synthesis to 2-aminofluorene, isolating one indenoquinoline.

2-Aminofluorene has two positions ortho to the amino group free, so that the quinoline isolated by Diels may be formulated as A or B.



A



B

No attempt was made to orientate this compound but it was suggested that ring closure had taken place at position 1.

Since Diels first applied the Skraup procedure to 2-aminofluorene, a number of other workers (2) have prepared py-substituted quinolines from this amine by well established methods. Only one of these compounds, an indenocarbethoxyquinolinol prepared by Bremer and Hamilton (3), has been orientated. An indenoisatin first prepared by Neish was orientated by Campbell and Stafford (4).

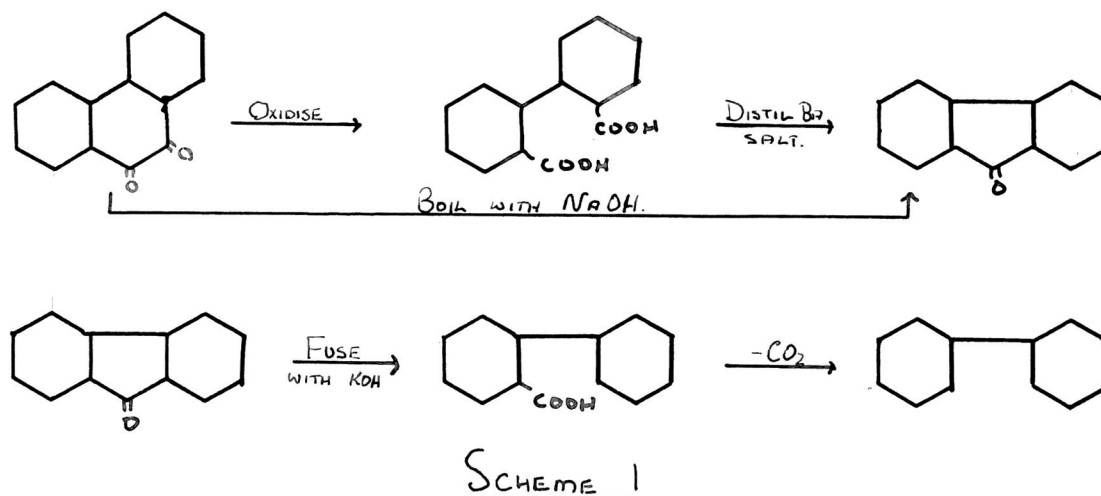
The object of this research was to establish the structure of the "Diels quinoline" and other substituted indenoquinolines.

A short section at the end of this thesis is devoted to the nitration of fluorene- and fluorenone-1-carboxylic acid.

INTRODUCTION

Before discussing the chemistry of 2-amino-fluorene, it is of interest to indicate the salient points in the chemistry of the hydrocarbon itself.

The hydrocarbon fluorene was discovered in crude anthracene oil (b.p. $300 - 310^{\circ}$) from coal tar by Berthelot in 1876 (5). On oxidation the hydrocarbon yielded a ketone (6), the structure of which was quickly established by synthesis from diphenic acid and from phenanthraquinone (7). By fusing with potassium hydroxide the ketone yielded an acid which decarboxylated to give the well known diphenyl (8). These reactions indicated the structure of the hydrocarbon to be biphenylenemethane. The reactions are summarised in scheme 1.

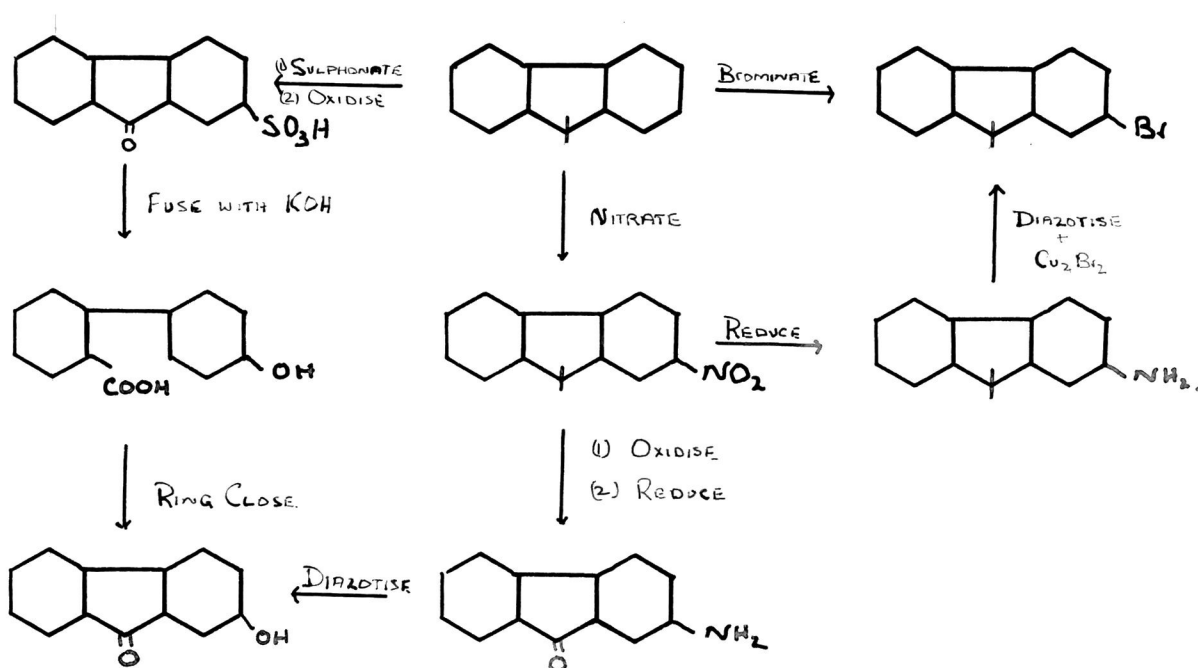


Fluorene undergoes attack at the 9-methylene group or in the diphenyl nucleus. Only the reactivity of the diphenyl nucleus is of interest at this point.

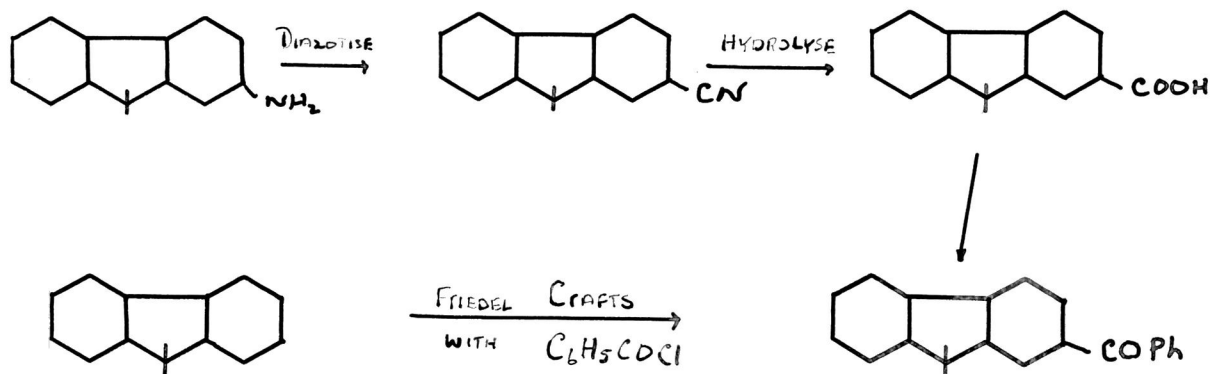
Monosubstitution/

Monosubstitution.

The monosubstitution of fluorene has been exhaustively studied by Courtot (9), who showed, as in scheme 2, the inter-relationship of a variety of mono substituted fluorenes.



The orientation of the above compounds was completed by the unambiguous synthesis of several 2-substituted fluorenes and fluorenones. The position of entry of the acetyl group in the Friedel Crafts reaction was shown by conversion of the acetyl compound to 2-acetamidofluorene by Beckmann rearrangement of the oxime (10). Fortner (11) orientated the benzoyl fluorene obtained by a Friedel Crafts reaction by synthesis from 2-carboxyfluorene as shown in scheme 3.



SCHEME 3.

Disubstitution

The position of entry into the fluorene molecule of a second group is dependent on the nature of the group already present. In some cases one disubstituted fluorene results, in others a mixture is obtained.

(a) Dibromination of fluorene gives 2:7-dibromofluorene only. The structure of this compound was shown by synthesis of its oxidation product from 2:7-dibromophenanthraquinone by the benzilic acid rearrangement (12).

(b) Nitration of 2-bromofluorene or bromination of 2-nitrofluorene yielded the same compound (9), which must be, because of the identity of the 2 and 7 positions 2-nitro-7-bromofluorene.

(c) Dinitration of fluorene gives a mixture of 2:5 and 2:7-dinitrofluorene (13). The structure of the latter was shown by synthesis of its oxidation product from 2:7-dinitrophenanthraquinone again by the benzilic acid rearrangement (12). The former product was considered to be either 2:4 or 2:5-dinitrofluorene since its oxidation product was different/

different from authentic 2:4-dinitrofluorenone and identical with the product of nitration of 4-nitrofluorenone. The only formulation consistent with the above facts is 2:5-dinitrofluorene.

(d) Diacetylation of fluorene has been shown to give 2:7-diacetylfluorene (14) for rearrangement of its dioxime yielded the known 2:7-diacetamidofluorene.

In the work described above emphasis has been placed on the substitution reactions of fluorene. Much of what has been said also applies to fluorenone since the presence of the keto group only serves to reduce the reactivity of the molecule, and not alter in any way the positions adopted by the substituents.

Polysubstitution of fluorene and fluorenone.

(a) A tribromofluorene obtained by the bromination of 2:7-dibromofluorene is known (15). The structure of this substance is not known with certainty but it is assumed to be 2:3:7-tribromofluorene. It has also been obtained by the Sandmeyer reaction on a compound assumed to be 3:7-dibromo-2-aminofluorene (16).

(b) A trinitrofluorenone obtained by boiling fluorenone with fuming nitric acid is described by Schmidt (15). Bell (17) obtained this compound by dinitrating 4-nitrofluorenone, this together with the fact that dinitration of fluorene leads to the 2:5 and 2:7 compounds, suggests the correct formulation/

formulation to be the 2:4-7.

A tetranitrofluorenone also obtained by Schmidt has been given the 2:4:5:7 formulation on the basis of the foregoing.

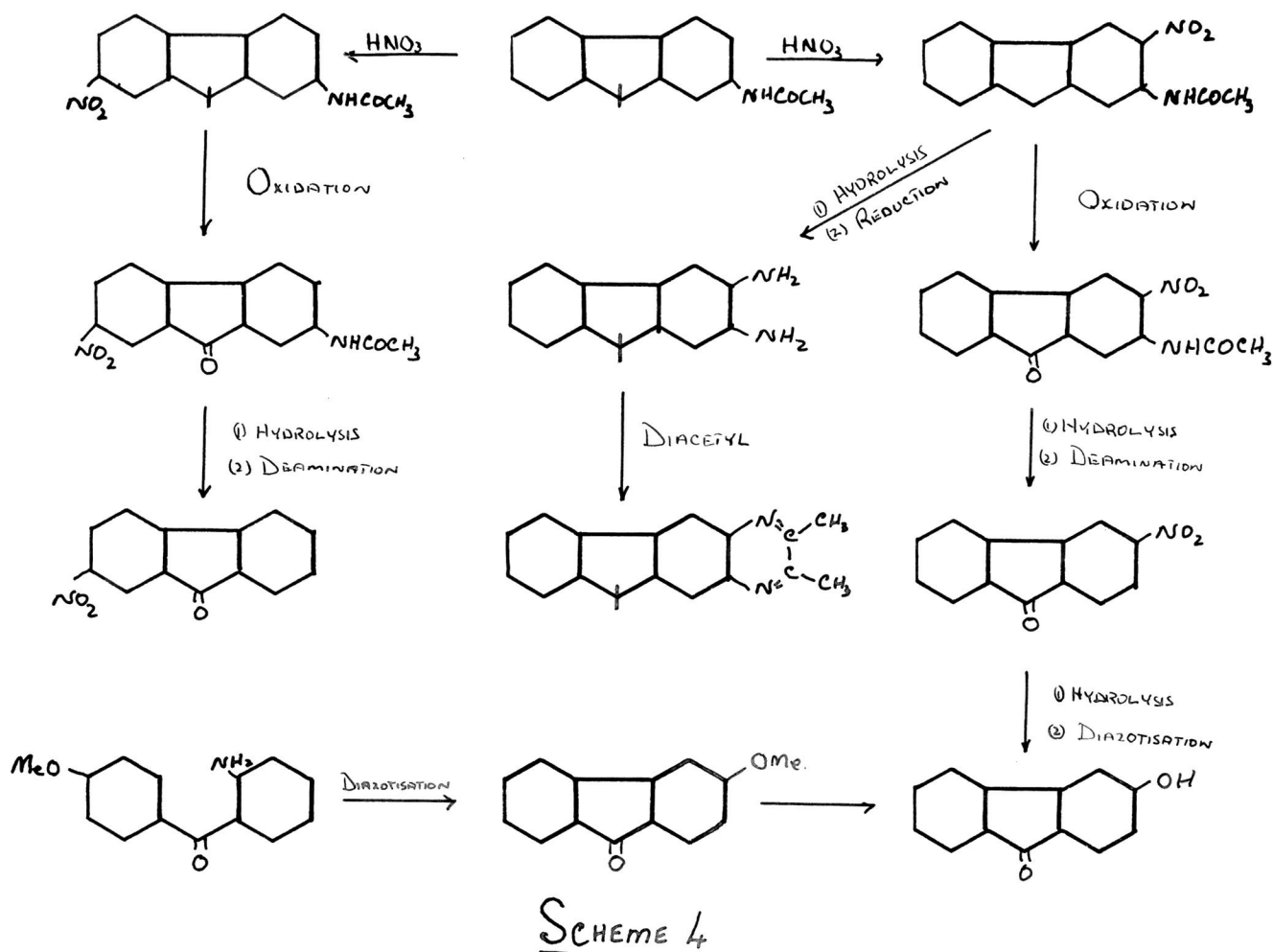
The substitution reactions of 2-aminofluorene.

These substitution reactions are of interest because use has been made of 3-substituted 2-aminofluorenes in attacking the problem of the orientation of the "Diels quinoline."

(a) The nitration of 2-acetamidofluorene:

This was first studied by Diels (18) who isolated a mixture of two nitroacetylaminos. The mixture was hydrolysed to the free amines and separated by means of their differing basicities. One of the compounds was shown to be 2-nitro-7-aminofluorene. The other was shown to be an o-nitramine for on reduction of the nitro group to amino, a compound with typical o-diamine reactions was obtained. Diels assumed this compound to be 1-nitro-2-aminofluorene. This formulation was accepted until Eckert and Langecker (19) disproved it in the following way. The nitroacetamidofluorene was oxidised to the corresponding fluorenone, which was then hydrolysed and deaminated to give a nitrofluorenone. This compound was reduced to the amine, and the amino group replaced by hydroxyl. The resulting hydroxyfluorenone was identical to a sample of 3-hydroxyfluorenone synthesised from 2-amino-4'-methoxybenzophenone. These/

These reactions are summarised in scheme 4.



(b) The bromination of 2-acetamidofluorene was shown by Campbell and Gilmore (20), to give in the first instance 2-bromo-7-acetamidofluorene which was known, and then a dibromo-2-acetamidofluorene. This compound on analogy with the nitration of 2-acetamidofluorene was designated 3:7-dibromo-2-acetamidofluorene. Bell (21) in studying the bromination of 2-N-tosylamidofluorene in chloroform isolated a monobromo compound, which on hydrolysis and acetylation was found to be different to 2-bromo-7-acetamidofluorene. On further bromination this substance gave the so called 3:7-dibromo-2-acetamidofluorene/

acetamidofluorene mentioned above. If this dibromo-2-acetamidofluorene is correctly formulated then Bell's compound must be 3-bromo-2-N-tosylamido-fluorene. Bromination of 2-N-tosylamidofluorene was studied in pyridine; this gave mainly the above 3-bromo compound with a small amount of an isomeric monobromo compound. Bell ascribed to this substance the 1-bromo-2-N-tosylamidofluorene formulation. Dibromination in this solvent gave a hitherto unknown dibromo-2-N-tosylamidofluorene which it was suggested was the 1:3 compound.

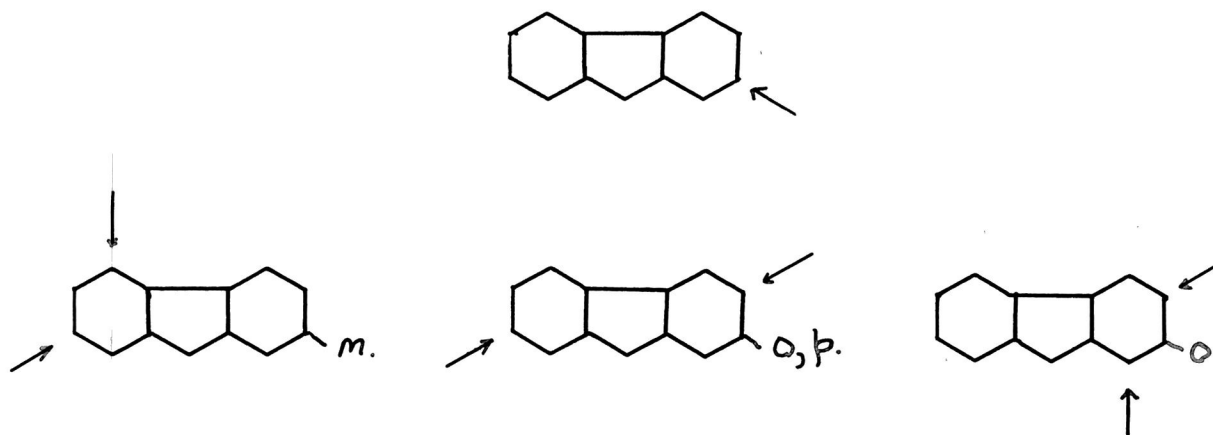
No attempt has been made to show without doubt the structures of these compounds described by Bell. Although the structures given to them are acceptable they must be regarded with some caution for, as yet, little is known about the availability of position 1 of the fluorene molecule for substitution.

Campbell and Keir (private communication) brominated 2-acetamido-7-nitrofluorene and obtained a monobromo-2-acetamido-7-nitrofluorene. Hydrolysis followed by removal of the amino group gave a bromo-7-nitrofluorene which was oxidised to the corresponding fluorenone. This substance was shown to be 3-bromo-7-nitrofluorenone by comparing with authentic 3-bromo-7-nitrofluorenone obtained from 12-bromo-4-nitrofluoranthene. Bromination must, therefore, have taken place at position 3, giving 2-acetamido-3-bromo-7-nitrofluorene.

Summary of the substitution reactions of
fluorene./

Summary of the substitution reactions of fluorene.

Monosubstitution occurs uniformly at position 2. The point of entry of a second group depends on the orienting effect of the group already present. With a meta directing group already present in the molecule a second group may enter the 7 or 5 position. When an ortho-para directing group is present positions 3 and 7 are next attacked. The strongly ortho directing tosylamido group is claimed to direct also to position 1.



The diagrams show the position of entry into the fluorene molecule when meta, ortho-para and strongly ortho directing groups are present at position 2.

Reactions of 2-substituted fluorenes involving positions 1 and 3.

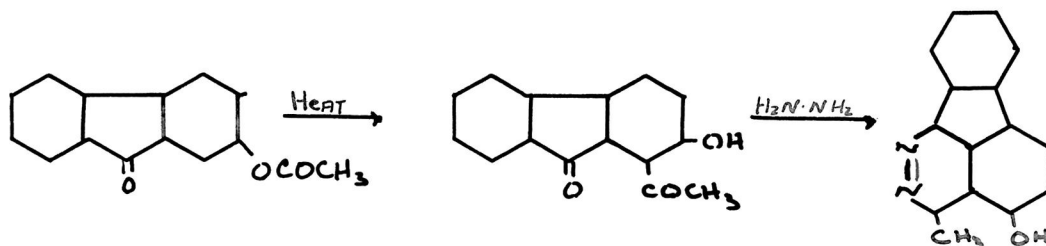
These reactions will be discussed under two main headings -

(a) The Fries and Claisen rearrangements, the Kolbe reaction.

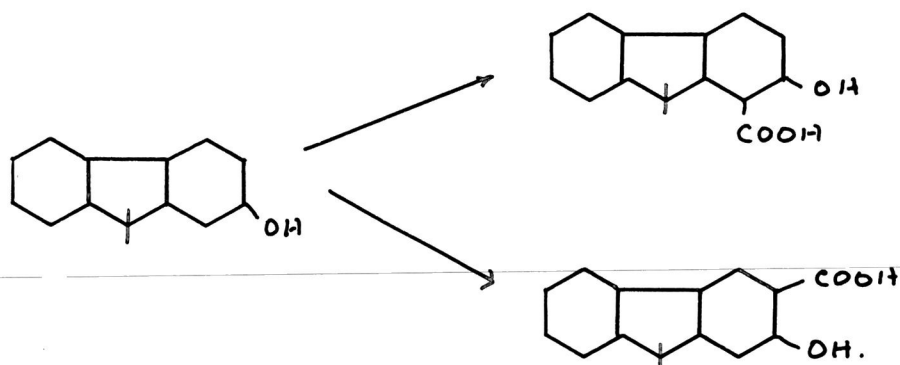
(b) Ring closure reactions.

(a) Lothrop (22) studying bond fixation in polynuclear/

polynuclear hydrocarbons, investigated the Claisen rearrangement of 2-fluorenyl allyl ether. On heating this substance at 235° a mixture of 1-allylfluoren-2-ol and 3-allylfluoren-2-ol resulted. Bergmann and Berlin (23) applied this reaction to 2-fluorenyl allyl ether and again obtained a mixture of the two possible products. The Fries (24) rearrangement was applied to 2-acetylhydroxyfluorenone giving a 15% yield of 1-acetyl-2-hydroxyfluorenone. The structure of the latter compound was shown by its reacting with hydrazine to give a diazafluoranthene.



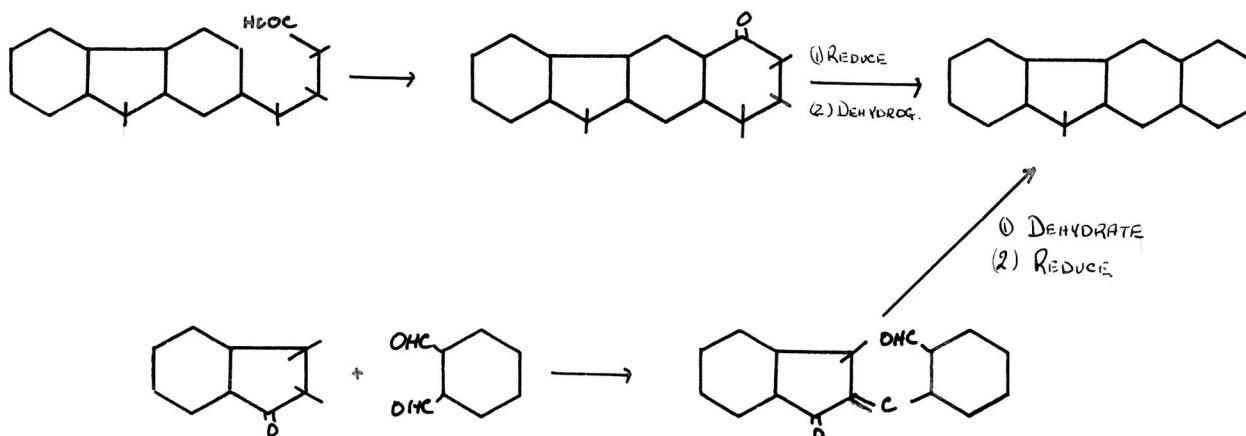
The Kolbe reaction with fluoren-2-ol is reported to give a mixture of the two possible indenosalicylic acids (25).



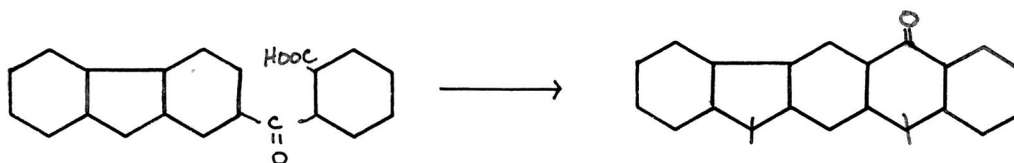
These experiments show that reaction can occur both/

both at the 1- and 3- positions.

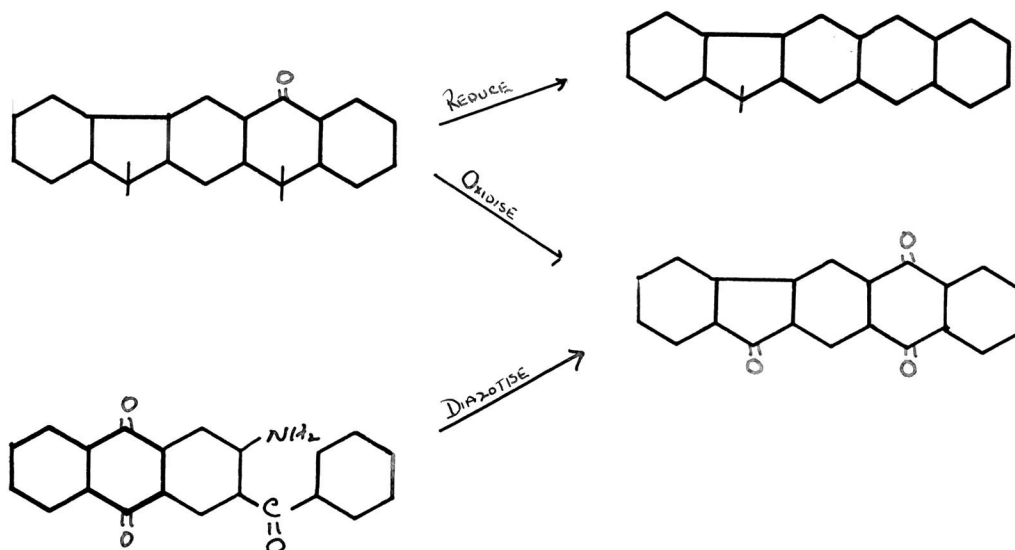
(b) Koelsh (26) required 1:2-benzfluorene as an intermediate and he attempted to prepare it by the Friedel Crafts ring closure of 2-fluorenyl- γ -propionic acid. The resulting ketone on reduction and dehydrogenation yielded the known 2:3-benzfluorene, which had been synthesised by Thiele (27) from α -hydrindone and o-phthalaldehyde as shown below.



Barnett et. al. (28) studying complex anthraquinones synthesised indeno-2':3'-2:3-anthracene. Fluorene was phthaloylated, the resulting phthaloylfluorene reduced with zinc and ammonia and then dehydrated to give an indenoanthrone. Reduction of the indenoanthrone gave the above indenoanthracene while oxidation gave an oxoindenoanthraquinone which was identical to that synthesised by Das Gupta (29), by the route shown below.

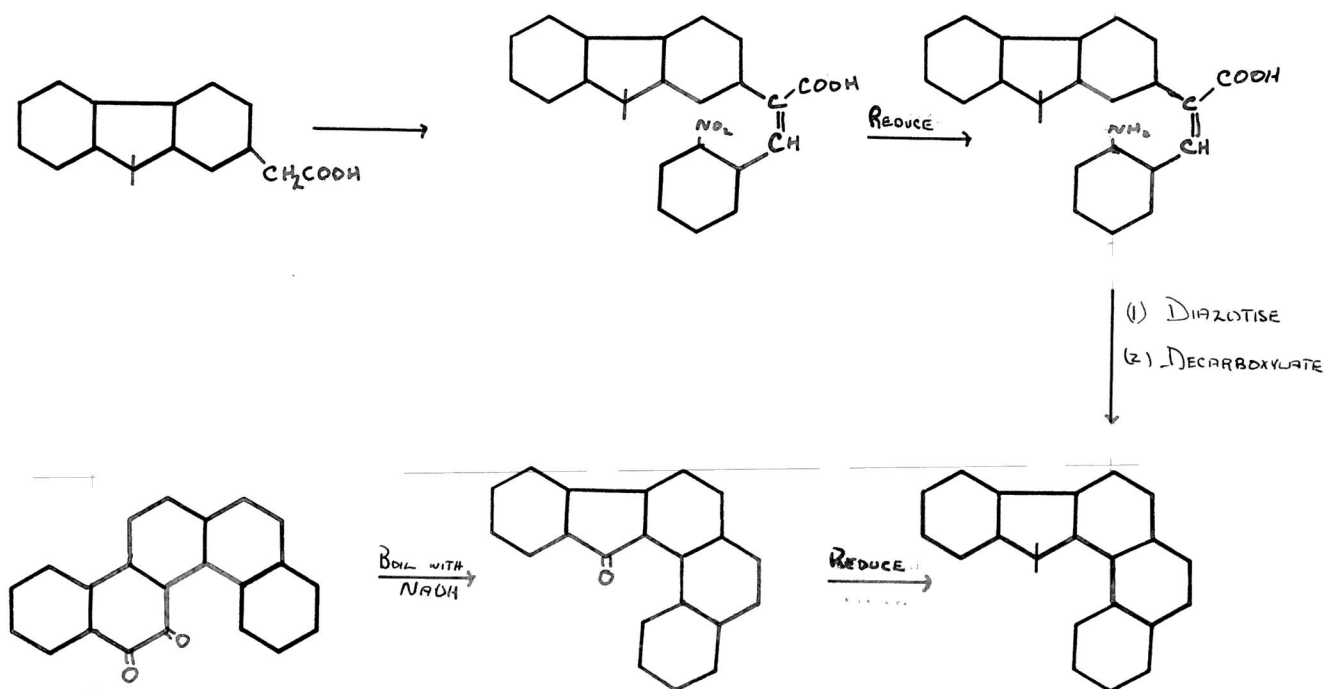


(12)



Ring closure had thus again taken place to position 3.

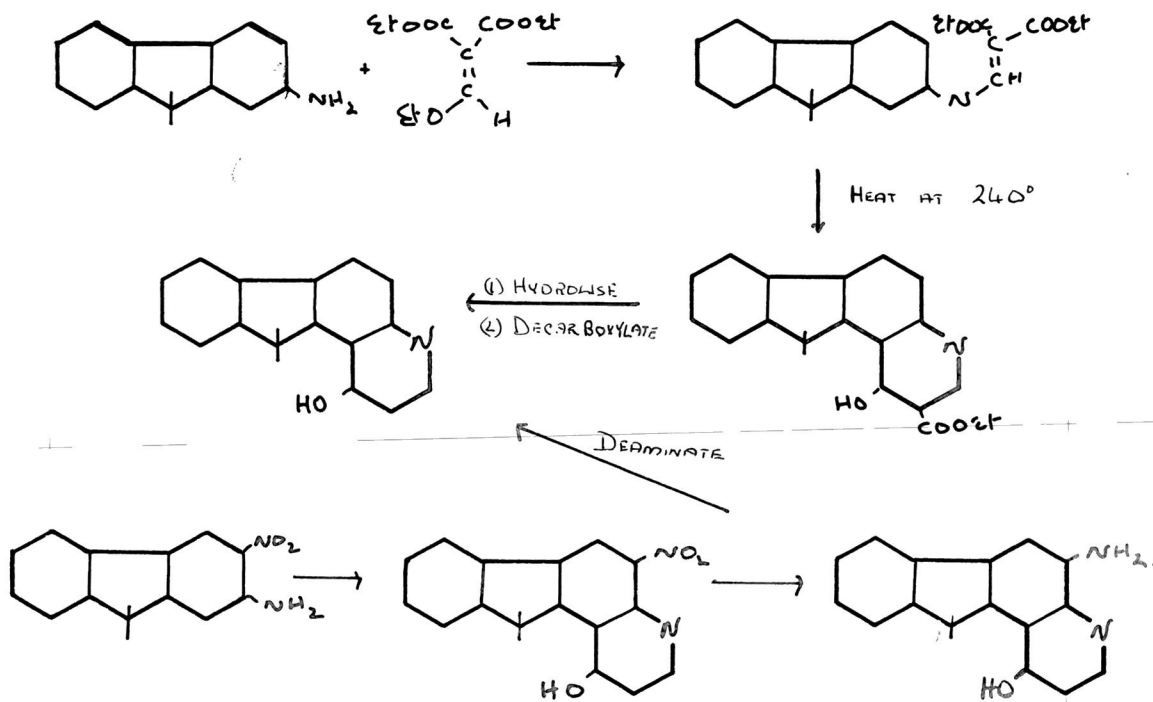
Cook (30) applied the Pschorr synthesis to fluorene-2-acetic acid expecting the ring closure to take place at position 3, as in the previous examples discussed. Ring closure, however, yielded a mixture of acids, the one which gave naphtho-1':2'-1:2-fluorene greatly preponderating. Ring closure had taken place mainly to position 1.



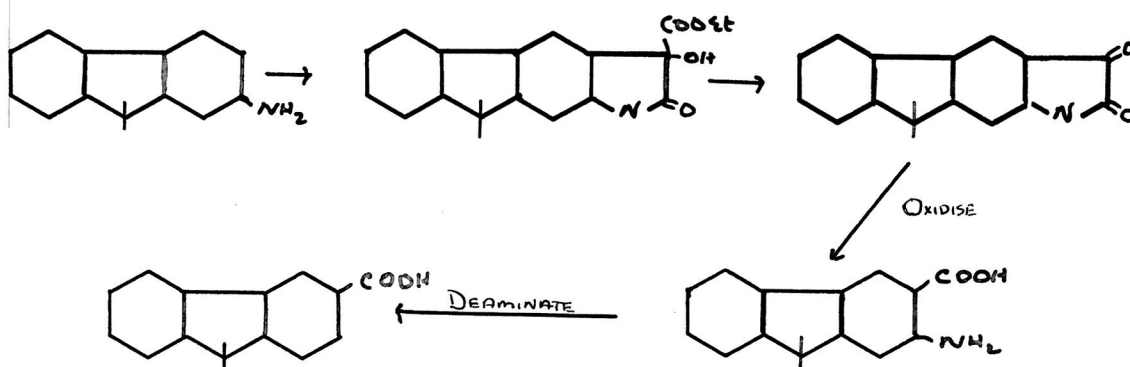
The structure of the ring closure product was shown by its synthesis from naphtho-1':2'-1:2-phenanthraquinone by the benzilic acid rearrangement, followed by reduction of the ketone.

Many ring closure reactions have been performed with 2-aminofluorene but in only two cases has the direction of ring closure been determined.

Bremer and Hamilton (3) condensed 2-aminofluorene with diethyl ethoxymethylenemalonate and then heated the product to 240° in diphenyl ether. Ring closure took place giving an indenocarbethoxyquinolinol which was hydrolysed and decarboxylated to give an indenoquinolinol. This sequence of reactions was applied to 3-nitro-2-aminofluorene, the product being then reduced and deaminated. The final product was identical with that obtained from 2-aminofluorene showing that ring closure had taken place in the first synthesis to position.1.



Neish (4) applied to 2-aminofluorene a method developed for the synthesis of isatins. 2-aminofluorene was boiled in alcohol with oxomalonate ester to give an indenocarbethoxydioxindole. This substance was easily oxidised, by aerating in alkaline solution, to an indenoisatin. Campbell and Stafford oxidised this compound to an indenoanthranilic acid with hydrogen peroxide. Deamination of the indenoanthranilic acid gave fluorene-3-carboxylic acid. In this case ring closure must have taken place to position 3 of the fluorene molecule.



At first sight the reactions discussed in this section appear to offer conflicting evidence with regard to the reactivity of the 1 and 3 positions in the fluorene molecule. It must be remembered, however, that the Pschorr synthesis when applied to β -naphthylacetic acid gave a mixture of the two possible benzphenanthrenes. β -Naphthalene derivatives show a much greater tendency to unidirectional cyclisation than might be expected with 2-substituted fluorenes. It is not, therefore, unreasonable to assume that a reversal of the "normal" direction of ring/

ring closure takes place when the Pschorr reaction is applied to 2-aminofluorene. If this view is accepted then a broad pattern of behaviour emerges. The reactions discussed in section (a) and one of the ring closure reactions were carried out at a high temperature (i.e. 200°). In each of these cases the principal reacting position was position 1. The remainder of the reactions described were carried out at a much lower temperature and in each case ring closure took place to position 3. Not enough data are available, however, to allow more to be made than the suggestion that temperature appears to be of prime importance in the direction of ring closure taken by derivatives of 2-aminofluorene. This immediately directs attention to the elucidation of the structure of the indeno-4-hydroxyquinoline obtained by Hughes and co-workers (2), for this compound was obtained by a high temperature cyclisation of β -(2-fluorenylamino)-crotonate. This quinolinol could not, unfortunately, be reduced by zinc dust distillation nor could it be converted to the corresponding chloro compound by means of phosphorus pentachloride. The difficulty of reducing this type of compound was also experienced by Clemo (31) who attempted to reduce Bremer and Hamilton's indenoquinolinol.

The next logical step in this study will be to try and direct any one ring closure reaction to the 1 and to the 3 position by altering the temperature at which the reaction is carried out.

The/

The following table shows all the compounds which have been prepared by ring closure reactions with 2-aminofluorene and whether or not the structure of the compound is known.

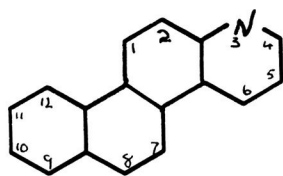
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DISCUSSION

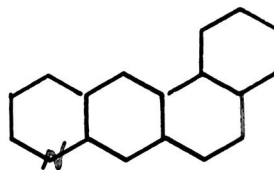
The problem of the structure of the "Diels quinoline" and the related compounds is one which might be attacked in two ways; by degradation or by synthesis.

Two ways of opening the nitrogen containing ring of the "Diels quinoline" were attempted. The first of these methods involved the well known Ende degradation. The value of this method is demonstrated by its application to 3-azachrysene, the structure of which assumes considerable importance later on in this work.

3-Azachrysene was first prepared by Mossetig and Kruger (32) by applying the Skraup reaction to 2-aminophenanthrene. Since this amine, like 2-aminofluorene has two free "ortho" positions, the quinoline obtained can have one of two possible formulations, (a) or (b) below.

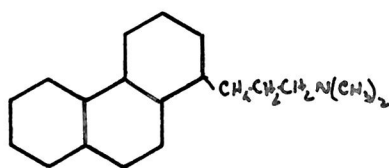


(a)

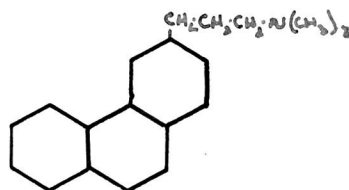


(b)

The product from the Skraup reaction was reduced catalytically to the 3:4:5:6-tetrahydro base, this was methylated and the quaternary salt reduced further with sodium amalgam. This resulted in opening of the nitrogen ring giving a compound which could be formulated as either w-dimethylamino-1-propylphenanthrene (c), or w-dimethylamino-3-propylphenanthrene (d).



(c)



(d)

The latter compound was synthesised unambiguously from 3-acetylphenanthrene and was found to be different from the product obtained by the Emde reduction on the quinoline, which must, therefore, be (c). Ring closure must have taken place to position 1 of the phenanthrene molecule giving 3-azachrysene (a).

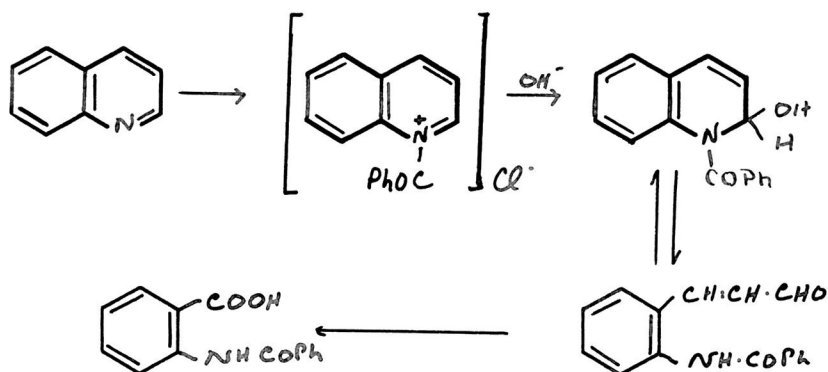
One of the most obvious approaches to establish the structure of "Diels quinoline" was to apply the Emde degradation and then to oxidise the side chain to a carboxyl group. The solution of the problem would then depend upon identifying the product as fluorene-1-carboxylic acid or fluorene-3-carboxylic acid, or possibly the corresponding fluorenone compounds, all of which are known.

2-Nitrofluorene was prepared in the way described in "Organic Synthesis" (33). Reduction of the nitro compound again as described in "Organic Synthesis" was attempted, but as had previously been found in this Department, was not satisfactory. An alternative method was sought. Catalytic reduction with Raney nickel in alcoholic solution was tried, but gave instead of the amine, 2:2'-azoxyfluorene. On the other hand reduction with finely reduced iron powder/

powder and hydrochloric acid in alcoholic solution gave excellent results. The success of this method depends on the ease with which the amine can be separated from the iron salts. The conditions were adjusted so that the amine hydrochloride was precipitated completely from the reaction mixture, treatment with alkali gave the amine only slightly contaminated with iron. Recrystallisation from alcohol gave the pure amine. The indenoquinoline was prepared as described by Diels (1); final purification of the product was achieved by chromatography.

Diels in his original paper described the reduction of the indenoquinoline with tin and hydrochloric acid to the 1:2:3:4-tetrahydroindenoquinoline. This reaction was attempted but could not be accomplished, the only product being an intractible oil. Reduction with sodium in ethanol and in amyl alcohol was investigated, but in each case an oil similar to that above was obtained. Failure to get the crystalline tetrahydro compound described by Diels led to the abandonment of this approach to the problem.

If quinoline is shaken with an alkaline solution of benzoyl chloride (34), N-benzoylquinolinium hydroxide is formed. This substance is in equilibrium with the isomeric benzoylaminocinnamaldehyde, which can be easily oxidised to benzoylanthranilic acid.



Application of this reaction to "Diels quinoline" would give 2-aminofluorene-1-carboxylic acid or 2-aminofluorene-3-carboxylic acid as the benzoyl derivative. The former of these compounds could be prepared by the reduction of the known 2-nitrofluorene-1-carboxylic acid (35), while the latter was prepared by Stafford (Thesis - Edinburgh) by the oxidation of 2':3'-6:5-indenoisatin.

This method was applied to "Diels quinoline", but it failed to react, unchanged starting material being obtained from the reaction mixture.

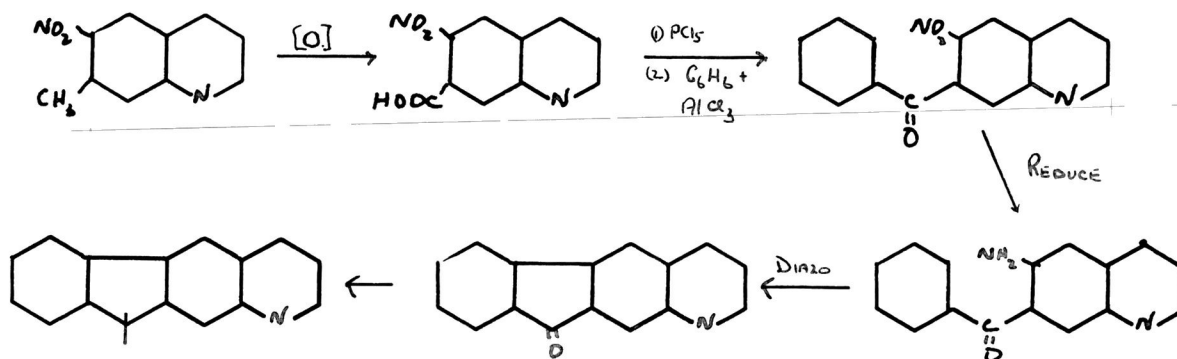
The possible routes to the unambiguous synthesis of either of the isomeric indenoquinolines are summarised under the following headings, each of which will be discussed.

- (1) From indene or hydrindone.
- (2) From a 5:6 or 6:7 disubstituted quinoline.
- (3) By blocking either the 1 or 3 position of 2-aminofluorene, then removing the blocking group after ring closing.
- (4) From a suitably substituted phenanthraquinone.
- (5)/

(5) From a 1:2 or 2:3 disubstituted fluorene.

(1) The available methods for the synthesis of substituted fluorenes from indene or a hydrindone involve Diels Alder addition to indene, or condensation of hydrindone with aldehydes or ketones followed by ring closure of the product. The first method does not permit the unambiguous synthesis of a substituted fluorene unless the diene is symmetrical. If the synthesis of an indenoquinoline was attempted in this way the diene would of necessity be unsymmetrical so that the method would not be unambiguous. The second method suffers from the same disadvantage and also because the necessary pyridine aldehydes or ketones are not easily available. An examination of these methods quickly showed their unsuitability for adaptation to the synthesis of indeno-2':3'-7:6-quinoline, or indeno-2':3'-5:6-quinoline.

(2) The possibility of synthesising either indenoquinoline from a disubstituted quinoline was investigated. The most promising synthesis appeared to be that of indeno-2':3'-7:6-quinoline from 6-nitro-7-methylquinoline, as indicated below.



6-Nitro-7-methylquinoline was first prepared by Huisgen (36) by applying the Skraup reaction to 6-nitro-m-toluidine. This amine was prepared by the method of McGooken and Swift (37), who obtained it by nitrating m-acetotoluidide. This reaction gave a mixture of 4 and 6-nitro-m-acetotoluidide which was hydrolysed to the free amines and then separated by fractional crystallisation from carbon tetrachloride. This method of separating the mixture is inconvenient because of the sparing solubility of the amines in carbon tetrachloride; benzene was found to be a much better solvent.

The Skraup reaction was applied to 6-nitro-m-toluidine following Huisgen's instructions. This reaction yields a mixture of 6-nitro-5-methylquinoline and 6-nitro-7-methylquinoline which Huisgen separated by fractional crystallisation from acetone. This method was found to be difficult and tedious due to the presence of tar in the reaction product. The following method was found to give excellent results. The crude mixture of quinolines was dissolved in hot dilute hydrochloric acid (charcoal), and then reprecipitated with alkali. The grey solid so obtained was dissolved in benzene and chromatographed on alumina. A colourless band developed and was eluted with benzene. Evaporation of the eluate to dryness yielded colourless needles melting at 118 - 119°. This appeared to be mixed crystals of the two quinolines. Separation of the two/

two isomers could be accomplished by chromatography. Separation on the large scale was achieved by making use of the fact that 6-nitro-5-methylquinoline on boiling in alcoholic potash oxidises to give 6:6'-dinitro-5:5'-diquinolylethane. The mixture was boiled in alcoholic potash during which the diquinolylethane separated. The solution was filtered and evaporated to small bulk. The residue was chromatographed in benzene to remove traces of the diquinolylethane and resinous material formed during the reaction. 6-Nitro-7-methylquinoline was thus produced in comparatively good yield.

The oxidation of this compound to 6-nitroquinoline-7-carboxylic acid was studied. Oxidation with sodium dichromate was tried. This reagent seemed depending on the conditions, either not to attack the quinoline or to completely destroy it, for starting material was obtained unchanged, or had disappeared completely. Attention was turned to a method worked out by Campbell and Learmonth (38), for oxidations of this type. The 6-nitro-7-methylquinoline was heated in a sealed tube with dilute nitric acid. Again no acidic substance could be isolated, starting material was returned quantitatively or not at all. Large quantities of gas were produced in reactions where no starting material was returned.

An attempt to tribrominate the methyl group of 6-nitro-7-methylquinoline following the method of Hammic/

Hammick(39), for the tribromination of quinaldine, was made. Quinaldine when boiled with bromine in acetic acid containing anhydrous sodium acetate, brominates in the methyl group. The tribromo-quinaldine hydrolyses with 10% sulphuric acid to give quinaldinic acid. 6-Nitro-7-methylquinoline was brominated under similar conditions to those described by Hammick. A substance of indefinite melting point was obtained which analysis showed contained two atoms of bromine. Attempts to hydrolyse this compound with 10% sulphuric acid were unsuccessful. In subsequent experiments the concentration of the sulphuric acid was raised to the point where charring began without effecting hydrolysis. Treatment with 10% sodium hydroxide resulted in the production of much resin. An attempt to brominate this substance further was unsuccessful. Although monobromo and dibromoquinaldine are very resistant to hydrolysis (40), it may be that this dibromoindenoquinaldine is substituted in the nucleus for it is usually impossible to stop bromination of this type at an intermediate stage. Nuclear bromination is not unlikely for 6-methylquinoline brominates not only in the methyl group but also in the nucleus, at position 3 (41). This route to indeno-2':3'-7:6-quinoline was abandoned at this point.

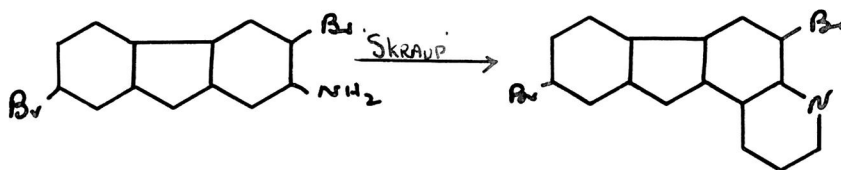
(3) One of the most promising methods of attacking the problem of the synthesis of either indenoquinoline appeared to be by blocking one of the/

the positions ortho to the amino group in 2-aminofluorene, applying the Skraup reaction and then removing the blocking group. This method of unambiguous synthesis has been applied successfully to several quinolines including the 4-hydroxy-2':3'-5:6-indenoquinoline prepared by Bremer and Hamilton. These workers applied their ring closure reaction first of all to 2-aminofluorene and then to 3-nitro-2-aminofluorene. Removal of the nitro group by reduction and deamination left them with the same compound as was obtained from 2-aminofluorene, thus showing ring closure to have taken place to position 1.

3-Nitro-2-aminofluorene was prepared by nitrating 2-acetamidofluorene (42), hydrolysing the mixture of 7-nitro and 3-nitro-2-acetamidofluorenes to the free bases and partially separating them by making use of their differing basicities. Final purification was achieved by chromatographing the impure 3-nitro-2-aminofluorene on alumina in xylene. The Skraup reaction was applied to 3-nitro-2-aminofluorene using conditions similar to those employed in the preparation of Diels quinoline. The reaction product, which was very tarry, was carefully worked up, again employing chromatography and yielded a very small amount of a pale yellow crystalline substance. Analysis of this substance did not agree with the theoretical for 8-nitroindeno-2':3'-5:6-quinoline, but indicated the compound to be 1'-oxoindenoquinoline./

oxoindenoquinoline. A mixed melting point with the product of oxidation of "Diels quinoline" showed no depression. The fact that the Skraup reaction with α -nitro- β -naphthylamine gives 5:6-benzoquinoline in place of the expected 8-nitro-6:7-benzoquinoline (43), suggests that removal of the nitro group in 3-nitro-2-aminofluorene was to accommodate ring closure to position 3. Oxidation of the fluorene to fluorenone during the reaction is not surprising for a small amount of the oxoindenoquinoline is always produced in the preparation of "Diels quinoline." Bell and Mulholland (private communication) had tried the above reaction but were unable to isolate any basic substance from the reaction product.

Mulholland (Thesis - Belfast) applied the Skraup reaction to 3:7-dibromo-2-aminofluorene and isolated in good yield a substance which analysed for 6':8-dibromoindeno-2':3'-5:6-quinoline.



This author then attempted in several ways to remove the bromine from this compound but without success.

Campbell and Gilmore (44) had investigated the removal of bromine from bromofluorenes and bromofluorenones/

fluorenones by heating these compounds in a sealed tube with pyridine and cuprous cyanide. In this way they were able to remove all the bromine from 2:7-dibromofluorene and 2:4:7-tribromofluorenone. It was also thought that it might be possible to remove bromine from this type of compound by reduction with red phosphorus and hydriodic acid. Accordingly 2-bromofluorene, 2:7-dibromofluorene, 2:3:7-tribromofluorenone and 3:7-dibromo-2-aminofluorene were treated with this reagent. It was found that bromine in the 2 and 2:7 positions were unattacked by this reagent, but bromine in the 3 position was removed. The yields in the cases where debromination took place were good. With the experience of Campbell and Gilmore and that just described it was felt that if the dibromoindenoquinoline prepared by Mulholland could be obtained, it would be possible to remove all the bromine, or at least the bromine in position 3 of the fluorene molecule.

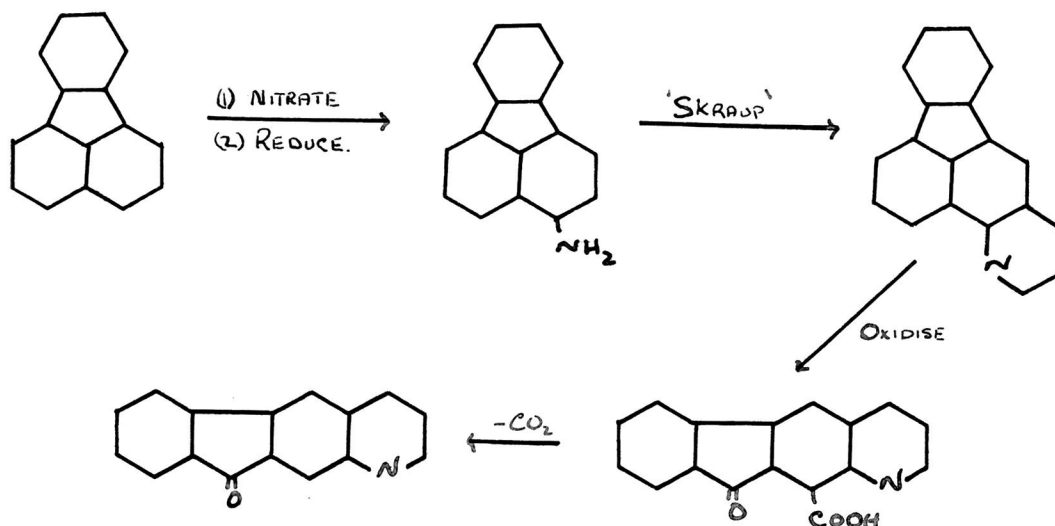
The preparation of 3:7-dibromo-2-aminofluorene was attempted in the following way. The p-toluenesulphonyl derivative of 2-aminofluorene was prepared and brominated by boiling with bromine in chloroform solution. Bell and Mulholland (45) describe the hydrolysis of the resulting 3:7-dibromo-2-tosylamidofluorene by dissolving in conc. sulphuric acid. This reaction could not be made to work, starting material was returned almost quantitatively. Difficulty/

Difficulty was also experienced by Gilmore (Thesis - Edinburgh) in hydrolysing this type of compound.

A more roundabout but more successful method is that of Gilmore. Fluorene was brominated in chloroform at 0° giving 2-bromofluorene. The separation of this substance from contaminating 2:7-dibromofluorene is a difficult and tedious process and was not attempted, for it was found that the contaminant could readily be removed at the next stage. The impure 2-bromofluorene was nitrated in glacial acetic acid, 2-bromo-7-nitrofluorene crystallising from the reaction mixture. Gilmore reduced this compound with zinc dust and alcohol. The method described earlier (p.19) for the preparation of 2-aminofluorene was preferred, and was applied successfully to this compound. Yields of 90 - 95% were easily achieved. The amine was acetylated in the usual way. Bromination of 7-bromo-2-acetamidofluorene was carried out by Gilmore in a mixture of chloroform and pyridine. This was attempted but found to be inconvenient on the moderately large scale due to the insolubility of the starting material in the mixed solvents. Bromination in nitrobenzene proved to be successful except that a tedious steam distillation was involved at the end of the experiment. The 3:7:dibromo-2-acetamidofluorene was hydrolysed smoothly to the amine with 60% sulphuric acid. The Skraup reaction was applied to this substance following the method of Mulholland but only a very small/

small quantity of the quinoline was obtained. The reaction was repeated using arsenic pentoxide as the oxidising agent in preference to the sodium m-nitrobenzenesulphonate used by Mulholland. Again only a very small yield of the quinoline was obtained. This material melted ten degrees lower than that quoted by Mulholland. Prof. Bell in a private communication stated that he too had repeated this experiment but had been unable to isolate any quinoline. The work of Mulholland is, therefore, suspect. The fact that only very small yields of quinoline were obtained from this amine again suggests that ring closure takes place preferentially at position 3 of the fluorene molecule.

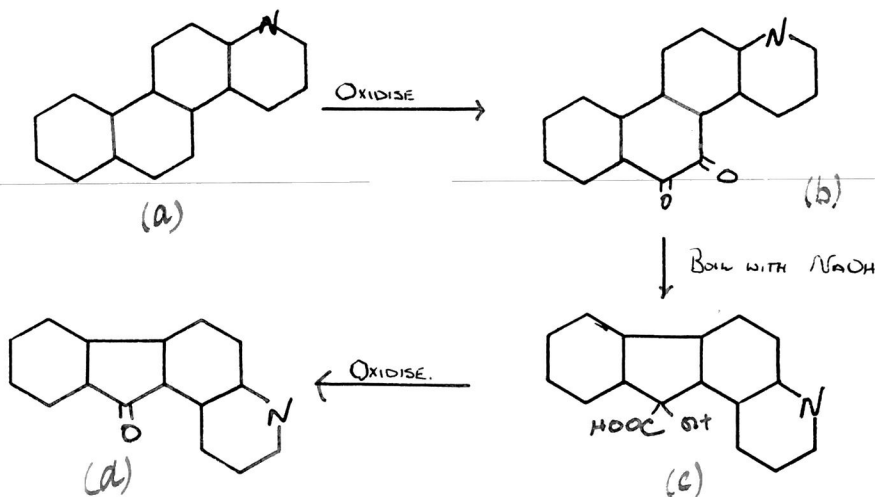
Since there are strong indications that ring closure takes place to position 3 of the fluorene molecule, an obvious method was to block position 1 of the fluorene molecule, and then apply the Skraup reaction. The only available 1-substituted-2-aminofluorene was 4-aminofluoranthene which can be regarded as 2-amino-1:9-benzofluorene. The Skraup reaction with this amine can only give 2':3'-4:3-pyridofluoranthene which should oxidise to give 1'-oxoindeno-2':3'-7:6-quinoline-8-carboxylic acid. Decarboxylation of this acid should give one of the required indenoquinolines. The scheme below indicates the sequence of reactions.



4-Nitrofluoranthene was prepared according to the directions of Gerty (Thesis - Edinburgh), and was obtained in 20% yield. Hydrogenation in acetic acid (A.R.) with Raney nickel as catalyst was found to be very convenient for the small quantities of nitro compound being reduced. The amine was isolated as its acetyl compound, purified as such, and then hydrolysed with sulphuric acid. The 4-aminofluoranthene so obtained was considered to be sufficiently pure for the subsequent Skraup reaction. The Skraup reaction was carried out with this amine under conditions similar to those employed with 2-aminofluorene. The reaction mixture on basification yielded a very small amount of basic material. This was chromatographed on alumina in benzene, yielding 2':3'-4:3-pyridofluoranthene as pale yellow prisms from light petroleum or pale yellow needles from alcohol, in 10% yield. The reaction was repeated using somewhat milder conditions with the same result./

result. Since fluocranthene sulphonates easily, it was thought that considerable sulphonation had taken place. Experiments were carried out with β -naphthylamine to find out if sulphuric acid in the Skraup reaction could be replaced with phosphoric or polyphosphoric acid. Small yields of 5:6-benzoquinoline were obtained but indicated that if the method was applied to 4-aminofluocranthene the yield would be no better than in the conventional procedure. Because of the smallness of the yields at the nitration and Skraup stage this promising line of attack had to be abandoned at this point.

(4) A synthesis which had been considered early in this work but which had been rejected on account of possible difficulties, was now carried out. It was proposed to synthesise 1'-oxoindeno-2':3'-5:6-quinoline from 3-azachrysene (a), a substance which has already been mentioned. The scheme was to oxidise the 3-azachrysene (a) to 3-azachrysene-7:8-quinone (b) and then apply the benzilic acid rearrangement. This would give a glycollic acid (c) which should oxidise easily to the required 1'-oxoindeno-2':3'-5:6-quinoline (d).



Mossetig and Kruger prepared 2-aminophenanthrene by the Beckmann arrangement of the oxime of 2-acetylphenanthrene. A more convenient method appeared to be from 2-acetylphenanthrene by the Schmidt reaction; this method was adopted.

Phenanthrene was acetylated in nitrobenzene (46) a mixture of 2- and 3-acetylphenanthrene resulting. The mixture was separated by making use of the large solubility differences of these substances in ether. The 2-acetylphenanthrene was treated with sodium azide in chloroacetic acid, a good yield of 2-acetamidophenanthrene being obtained. This reaction is much more easily carried out than the Beckmann rearrangement of the oxime as described by Mossetig and Kruger. Hydrolysis of the 2-acetamidophenanthrene was achieved conveniently with hydrochloric acid in ethanol. The Skraup reaction was carried out according to the method of Mossetig and Kruger, who claimed an 80 - 90% yield. These authors preferred the use of nitrobenzene as oxidising agent, but this involves removing aniline and unchanged nitrobenzene at the end of the reaction. The use of arsenic pentoxide simplified the working up procedure, and was used in a repetition of this experiment. The maximum yield obtained in either method was 70%.

The oxidation of 3-azachrysene was investigated. The conventional chromic acid oxidation for a period of one hour resulted in almost complete destruction of/

of the molecule; a trace of a red compound crystallising in needles was obtained. Progressively milder conditions were tried until it was found that boiling the 3-azachrysene with chromic acid in acetic acid for three minutes gave the best yield of quinone, which was about 15%. The quinone crystallised from xylene/petrol or could be sublimed under high vacuum, as crimson needles. Fortunately the benzilic acid rearrangement with this quinone went easily and smoothly so that the small quantities available were sufficient. The quinone was suspended in 10% caustic potash solution and heated on a water bath at 90 - 100°. After about three hours' heating it was noticed that the crimson needles of the quinone were being replaced by golden yellow needles. The expected product of this reaction, a glycollic acid should be soluble in the alkali, and so it was assumed that oxidation was taking place through to the fluorenone. A stream of air was bubbled through the reaction in order to help the process of oxidation. When the quinone had completely disappeared the yellow material was removed and purified by recrystallisation from methanol. Analysis showed this substance m.p. 178 - 179° to be 1'-oxoindeno-2':3'-5:6-quinoline. It considerably depressed the melting point of the product of oxidation of "Diels quinoline" m.p. 190°. If the structure of this substance was in fact 1'-oxoindeno-2'3'-5:6-quinoline then "Diels quinoline" must be indeno/

indeno-2':3'-7:6-quinoline.

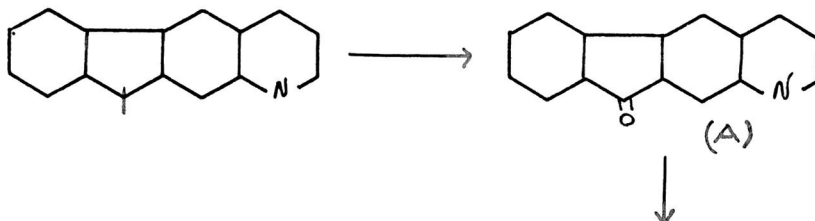
The weak link in the argument is the structure assigned to the quinone since it might be argued that oxidation had taken place at position 1 and 2 of the chrysene molecule giving 3-azachrysene-1:2-quinone. The product from the benzilic acid rearrangement would then be 1-aza-7:8-benzfluorenone. It was, therefore, necessary to prove the structure of the quinone.

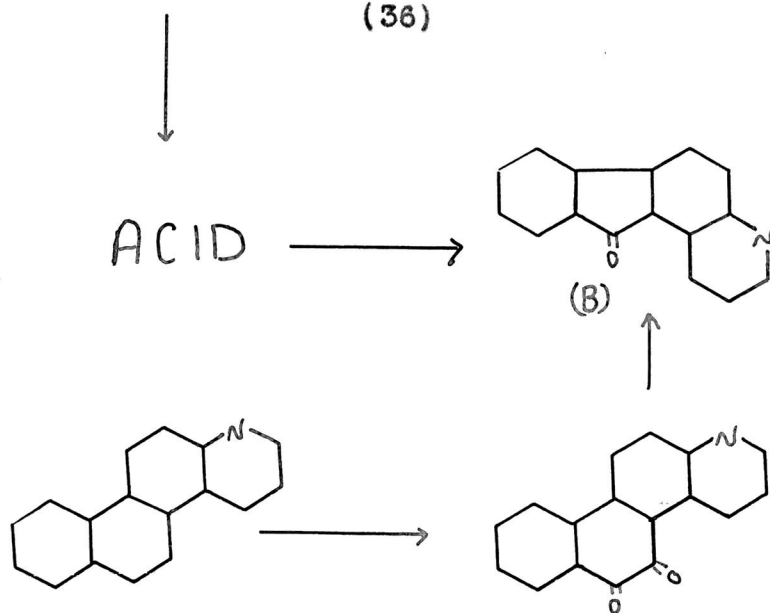
"Diels quinoline" was oxidised to the corresponding oxoindenoquinoline (A), ring opened to give an acid which on treating with conc. sulphuric acid gave back a different oxoindenoquinoline (B). This series of reactions when applied to either of the two quinolines theoretically obtainable by applying the Skraup reaction to 2-aminofluorene, could only give starting material back, or the other oxoindenoquinoline.

The product (B) was not identical with the oxoindenoquinoline started with and so must be the isomer.

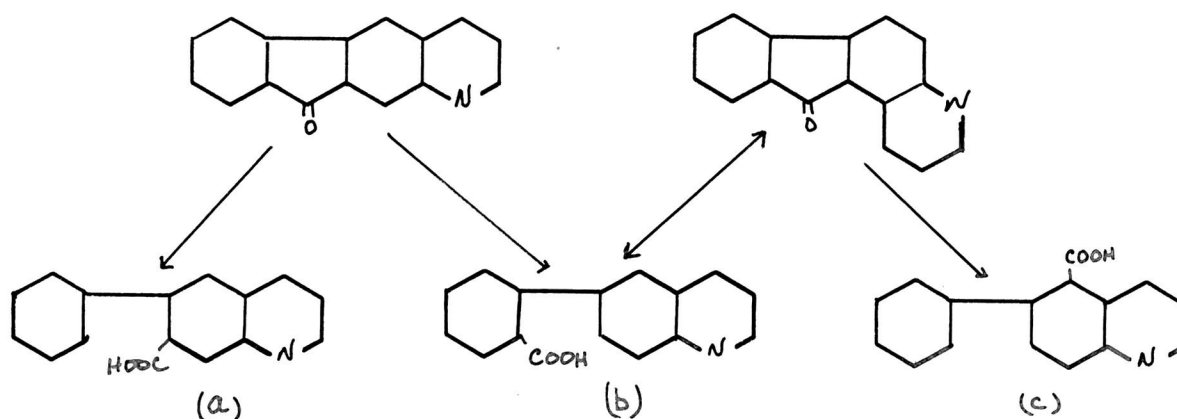
It was found to be identical with the benzilic acid rearrangement product which must be 1²-oxoindeno-2':3'-5:6-quinoline and not 1-aza-7:8-benzfluorenone.

The structure of the azachrysenequinone is, therefore, proved and the only possible formulation for "Diels quinoline" is indeno-2':3'-7:6-quinoline. The reactions are summarised in the scheme below.





The ring closure of the intermediate acid (b in the scheme below) in itself provides good, although not indisputable evidence for the structure of "Diels quinoline." In his original work in this field Diels oxidised the indenoquinoline, and then opened the five membered ring by fusing with caustic potash. One acid was obtained which could be one of three possible acids, depending on the structure of the quinoline and the way in which the ring opened.



The acids (a) or (c) above could only ring close to give back starting material in each case. In the case of the acid (b) ring closure would probably take place at position 5 of the quinoline nucleus since/

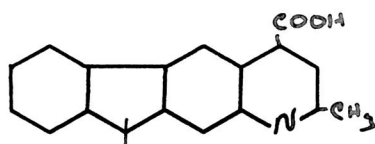
since this position is very much more reactive than position 7, The acid, as has been seen, did ring close to give an indenoquinoline different from the starting material and must, therefor, be (b). If ring closure of this acid can be assumed to take place at position 5 of the quinoline nucleus then the product must be 1'-oxoindeno-2':3'-5:6-quinoline and the oxidation product of "Diels quinoline," 1'-oxoindeno-2':3'-7:6-quinoline.

The ketone obtained by oxidising "Diels quinoline" was dissolved in diphenyl ether and treated with caustic potash. The acid, isolated as its potassium salt, was treated with cold concentrated sulphuric acid. The solution was warmed on a steam bath for 1 hour after which it was poured into cold water and basified. A golden yellow material was precipitated and was removed and recrystallised from methanol. This substance was found to be identical with the product obtained from the benzilic acid rearrangement on the azachrysenequinone.

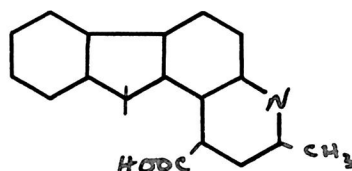
1'-Oxoindeno-2':3'-5:6-quinoline, obtained from "Diels quinoline," was reduced by the Huang Minlong modification of the Wolff Kishner reaction giving a disappointing small yield of a colourless substance melting at 145°.

Early in this work attention was turned from the indenoquinoline of Diels to the indenoquinaldine-4-carboxylic acid prepared by Neish (47). This worker applied the Doebner pyruvic acid synthesis to/

to 2-aminofluorene and isolated an acid, $C_{18}H_{13}NO_2$ which may be formulated as (a) or (b).



(a)



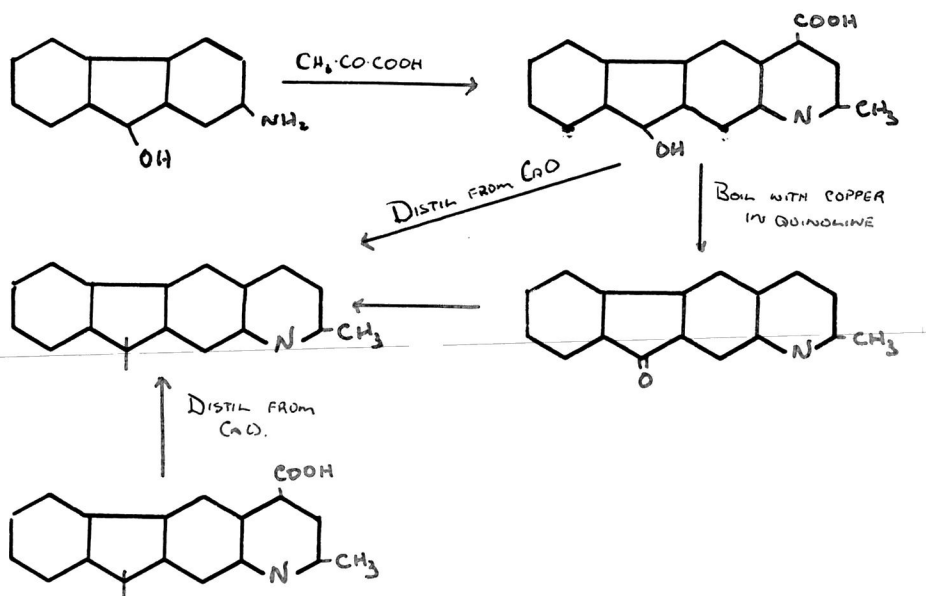
(b)

Without supporting evidence this author suggested the correct formulation to be (b). If this is in fact the case, it was thought that it might be possible to form a lactone ring between the carboxyl group and a hydroxy group on position 1'. Efforts were made to introduce a hydroxyl group at this point in the molecule. The acid itself was prepared by boiling 2-aminofluorene with pyruvic acid in ethanol. This acid is very high melting and very sparingly soluble in the common organic solvents. Oxidation with chromic acid in glacial acetic acid was attempted but due to the difficult solubility of the starting material and the product no pure substance could be isolated. To surmount this difficulty the Doebner pyruvic acid synthesis was applied to 2-amino-9-fluorenol. The product was again very high melting and was found impossible to purify. This acid was characterised as its methyl ester. Because of the difficulty in working with these acids no further work was done in this direction.

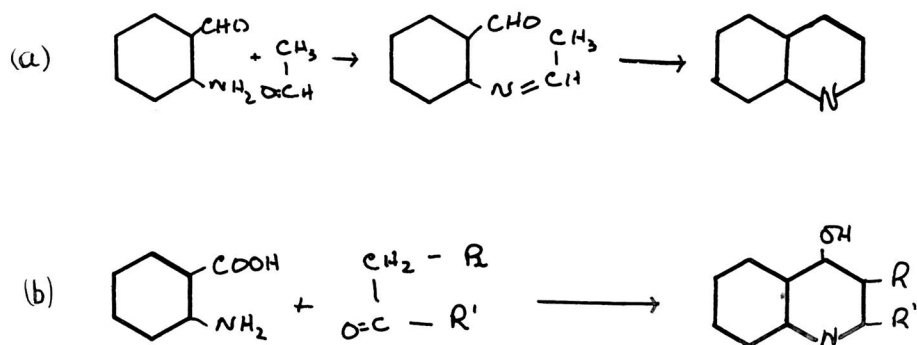
Neish's indenoquinaldine-4-carboxylic acid was esterified in three different ways; by boiling with methanol/

methanol and conc. sulphuric acid, by boiling in methanol and passing in HCl gas, and finally with diazomethane. The latter method was found to give the best yields of ester. The decarboxylation of this acid was best accomplished by distilling from lime, the conventional copper and quinoline method giving poorer yields and involving a much more tedious working up process.

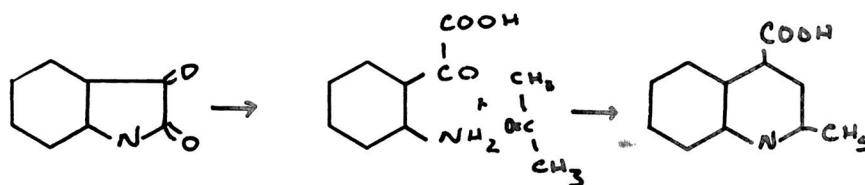
The decarboxylation of the ring closure product of 2-amino-9-fluorenone was attempted in two ways. By boiling in quinoline with copper bronze, a yellow substance crystallising in needles was obtained. Analysis of this substance suggested it to be an oxoindenoquininaldine rather than the hydroxyindenoquininaldine, and preparation of a dinitrophenylhydrazone confirmed this. Decarboxylation by distilling from lime gave surprisingly the indenoquininaldine obtained by decarboxylating Neish's indenoquininaldine-4-carboxylic acid. These reactions are summarised below.



The possibility of synthesising indeno-2':3'-7:6-quinaldine-4-carboxylic acid unambiguously was explored. Several methods for the synthesis of quinolines from o-substituted amines are known. Of these the Friedlander synthesis from o-aminobenzaldehyde (a), and Niewentowski's synthesis from anthranilic acid (b) are typical.



The difficulty, however, in preparing the o-substituted amines limits the usefulness of these reactions. 2-Nitrofluorenone-1-carboxylic acid, prepared by the oxidation of 4-nitrofluoranthene (35) is known, but is difficult to obtain in any reasonable quantity. A scheme of synthesis based on this substance was, therefore, rejected. The only other suitable substance available for a synthesis of this type is the indenoisatin first prepared by Neish (4). Isatin when dissolved in alkali ring opens to give the so called isatic acid, which is o-aminophenylglyoxylic acid. This substance readily condenses with aldehydes and ketones to yield substituted quinolines.



This reaction was devised by Pfitzinger and is named after him. The intention was, therefore, to prepare 2':3'-6:5-indenoisatin and apply the Pfitzinger reaction with acetone, which should give indeno-2':3'-7:6 quinaldine-4-carboxylic acid.

Oxomalonate ester was prepared in good yield according to the directions in "Organic Synthesis (48)". The ring closure with 2-aminofluorene and subsequent oxidation were carried out as described by Neish. During the oxidation a yellow crystalline substance separated out which appeared to be the sodium salt of the isatic acid. On boiling this substance in acetic acid with hydrochloric acid the isatin was obtained. If the oxidation was carried out by heating in alcoholic KOH solution instead of in aqueous NaOH, the isatin could be obtained directly.

The Pfitzinger reaction with this compound was carried out by boiling the isatin in alkaline solution with acetone. During the reaction time the greenish blue colour of the isatic acid turned to a deep golden brown. On acidifying the solution a brown amorphous substance was obtained which melted over the range 250 - 300°. Since difficulty had been/

been experienced in purifying the acids obtained by the Doebner reaction on 2-aminofluorene and 2-amino-9-fluorenol, it was decided to attempt to esterify this material and isolate the acid as its ester. The crude material was boiled in methanol containing 10% sulphuric acid. On working up the merest trace of a substance melting $150 - 157^{\circ}$ was obtained. The reaction was repeated and esterification attempted by bubbling HCl gas through a methanolic suspension of the crude product. A slightly larger quantity of the ester was obtained (2 - 3 m.g.) but could not be purified completely; in its impure state it melted $154 - 159^{\circ}$. The reaction was repeated several times but it was found impossible to isolate sufficient of the ester to effect complete purification. The reaction was tried with acetone oxime replacing acetone but this did not improve the quality of the product. The Pfitzinger reaction was then attempted with pyruvic acid in place of the acetone. A high melting substance was obtained which appeared to consist mainly of resin. A small amount of an acidic substance was sublimed out of this product, but once again it was found difficult to purify.

The presence of a reactive methylene group in the isatin molecule probably assists in the formation of much of the resinous material produced in these reactions. With this in mind it was decided to repeat the whole synthesis with 2-aminofluorenone.

2-Aminofluorenone was prepared by reduction of 2-nitrofluorenone with sodium sulphide in preference to H_2S as was employed by Diels (49). Treatment with oxomalic ester in the same way as with 2-aminofluorene gave the corresponding dioxindole (3-carbethoxy-1'-oxoindeno-2':3'-6:5-dioxindole) but in poor yield. The poorness of the yield was probably due to the deactivating effect of the keto group. Because of the poorness of the yield of dioxindole the synthesis was abandoned.

As will be seen, subsequent work showed that the ring closure in the Doebner pyruvic acid synthesis had taken place at position 3 of the fluorene molecule. The impure compound isolated from the Pfitzinger reaction on 2':3'-6:5-indenoisatin with acetone must, therefore, have been the required ester. It is unfortunate that insufficient of this material was obtained for complete identification.

An effort was now made to decide the structure of some of the py-substituted indenoquinolines by removing the substituent groups and comparing the product with authentic indeno-2':3'-5:6-quinoline and indeno-2':3'-7:6-quinoline.

The Doebner-Miller reaction was applied to 2-aminofluorene by Hughes and co-workers (2), who isolated a substance quoted as melting $133 - 135^\circ$ in one part of their paper and $145 - 159^\circ$ in another part. The reaction was repeated according to their instructions, except that purification of the product was/

was effected by chromatography. The indenoquinaldine so obtained melted at 163° and was found to be identical with the product obtained by decarboxylating Neish's indenoquinaldine-4-carboxylic acid. The yield obtained in the Doebner-Miller reaction was only 10%; the best method of obtaining this substance is by decarboxylation of Neish's indenoquinaldine-4-carboxylic acid.

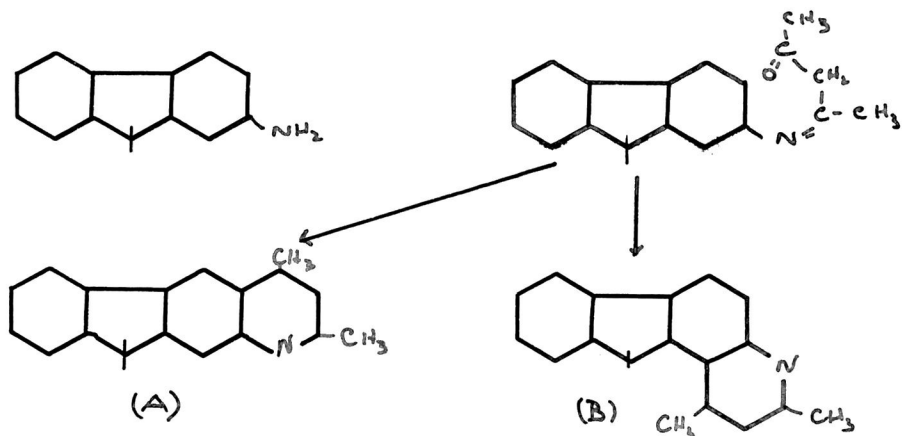
The indenoquinaldine was oxidised to the indenoquin aldehyde by boiling in dioxan with freshly prepared selenium dioxide. The use of freshly prepared selenium dioxide seems to be vital to the success of this reaction for Kaplan (50), on treating quinaldine with aged selenium dioxide obtained not the desired aldehyde, but quinaldoin, a substance analogous to benzoin. The major difficulty in this reaction was removal of the precipitated selenium. Boiling the dioxan with charcoal removed some of the selenium; the dioxan was then removed and the residue dissolved in alcohol, and boiled with a small amount of mercury. After boiling for 1 hour, charcoal was added and the boiling continued for a few more minutes. Hot filtration gave a colourless solution which deposited the aldehyde as colourless needles. The indenoquin aldehyde was oxidised to the acid by boiling in acetone with hydrogen peroxide. Evaporation to dryness gave the acid as yellow needles which were recrystallised from acetic acid. Decarboxylation of this acid was easily achieved by distillation/

distillation from calcium oxide. The product purified by chromatography and recrystallised from benzene/light petroleum was found to be identical with the Diels quinoline. It follows that ring closure in the Doebner-Miller and Doebner pyruvic acid synthesis must have taken place at position 3 of the fluorene molecule giving indeno-2':3'-7:6-quinaldine, and indeno-2':3'-7:6-quinaldine-4-carboxylic acid respectively.

The Combes synthesis was applied by Buu-Hoi (2), who condensed 2-aminofluorene with acetylacetone and cyclised the resulting Schiff's base by heating with conc. sulphuric acid. This work was repeated but with somewhat different results from those claimed by this author. On pouring the sulphuric acid solution into water a gelatinous precipitate appeared. This material completely dissolved in alkali and reappeared on acidification with sulphuric acid, while on acidifying with hydrochloric acid no precipitate was obtained. The most reasonable explanation of these facts appears to be that the compound had undergone sulphonation. The gelatinous precipitate would then be the sulphate of the sulphonated quinoline which would be soluble in alkali. On treatment of the alkaline solution with hydrochloric acid no precipitate was obtained because the hydrochlorides of these bases are much more soluble than the sulphates. It is, perhaps, significant that Hughes (2) applied this reaction to/

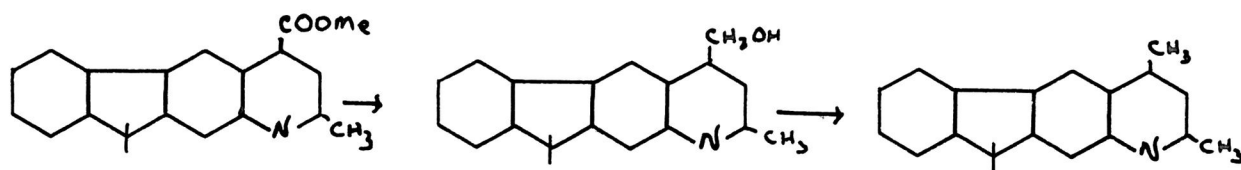
to 2-aminofluorenone, which is more difficult to sulphonate than 2-aminofluorene, but does not describe its application to 2-aminofluorene.

Since the ring closure could not be effected by the use of sulphuric acid, polyphosphoric acid was tried. A solution of polyphosphoric acid was made by dissolving phosphorus pentoxide in glacial phosphoric acid. The Schiff's base was added to this solution and the whole heated for two hours. Pouring the mixture into water and basifying gave the quinoline in good yield. This method suffers from one major disadvantage; the proportion of polyphosphoric acid required is much too great for application on anything greater than the 1 - 2 g. scale.

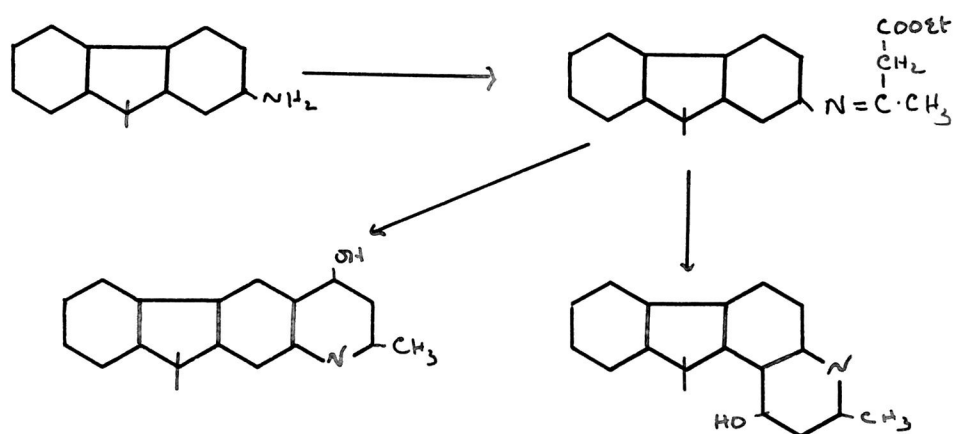


The structure of the 2:4-dimethylindenoquinoline (A) or (B) was shown by its unambiguous synthesis from indeno-2':3'-7:6-quinaldine-4-carboxylic acid. The methyl ester of this acid was reduced with lithium aluminium hydride to 4-hydroxymethylindeno-2':3'-7:6-quinaldine. This substance was reduced to 2:4-dimethylindeno-2':3'-7:6-quinoline by distilling/

distilling from zinc dust. An effort was made to replace the hydroxyl group using phosphorus tri-chloride, but this treatment led to the production of much tar and no crystalline substance. If this chloro compound had been obtained it would, no doubt, have reduced easily with lithium aluminium hydride. The less elegant zinc dust distillation, however, gave the required compound in 20% yield. A mixed melting point showed this compound to be identical to that obtained by the Combes synthesis on 2-aminofluorene.



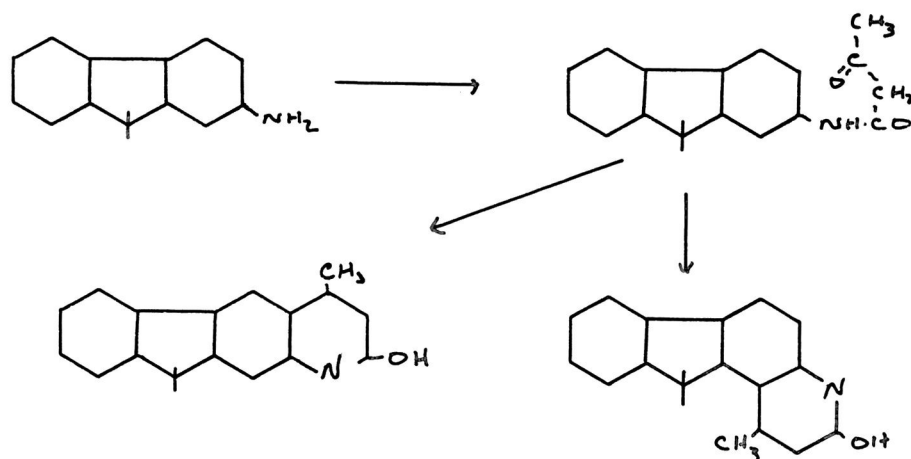
The Conrad Limpach synthesis was applied to 2-aminofluorene by Hughes (2).



An attempt to remove the hydroxyl group was made in order to compare the product with authentic indeno-2':3'-7:6-quinaldine. The reaction was carried as described by Hughes. The hydroxy indenoquinaldine was/

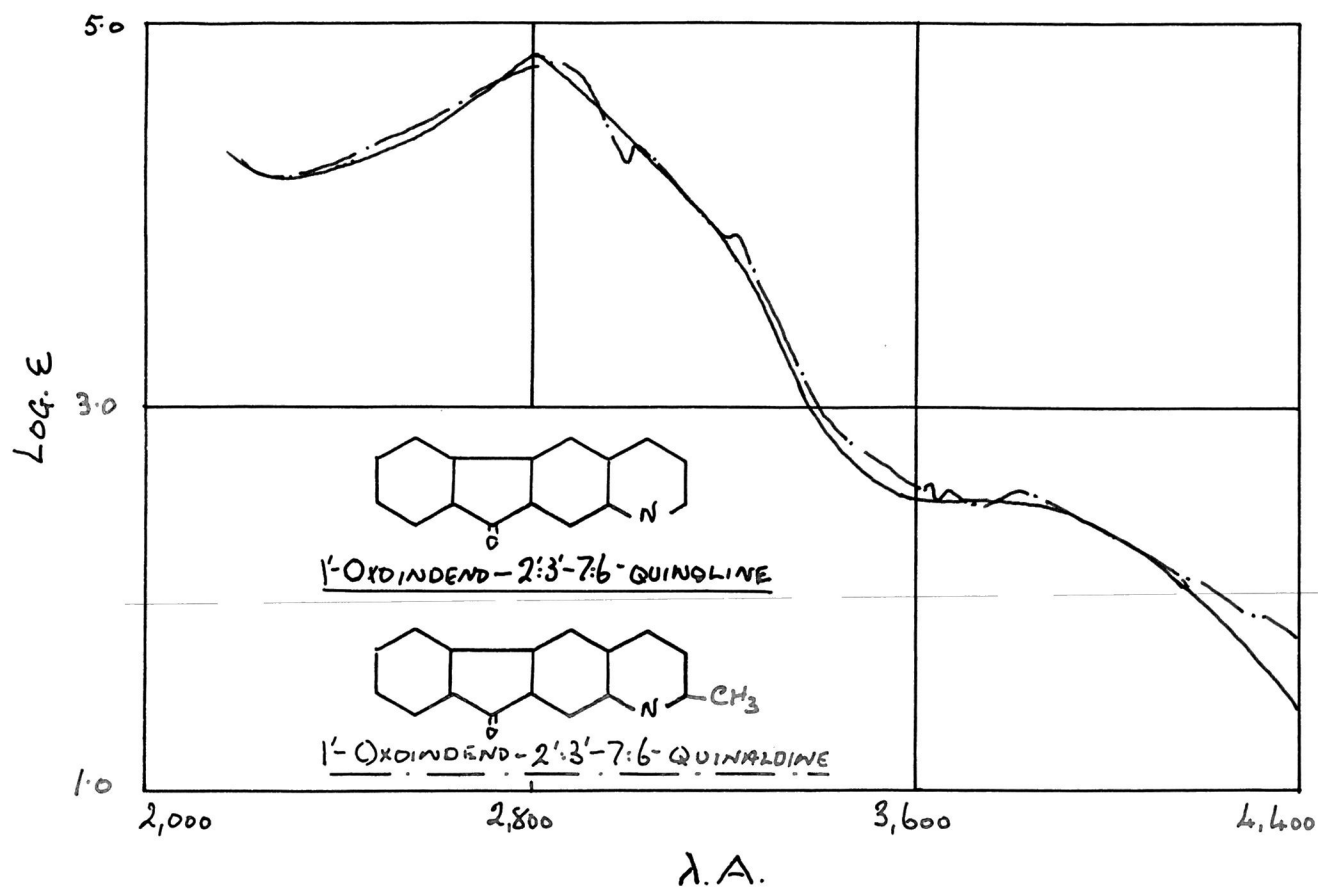
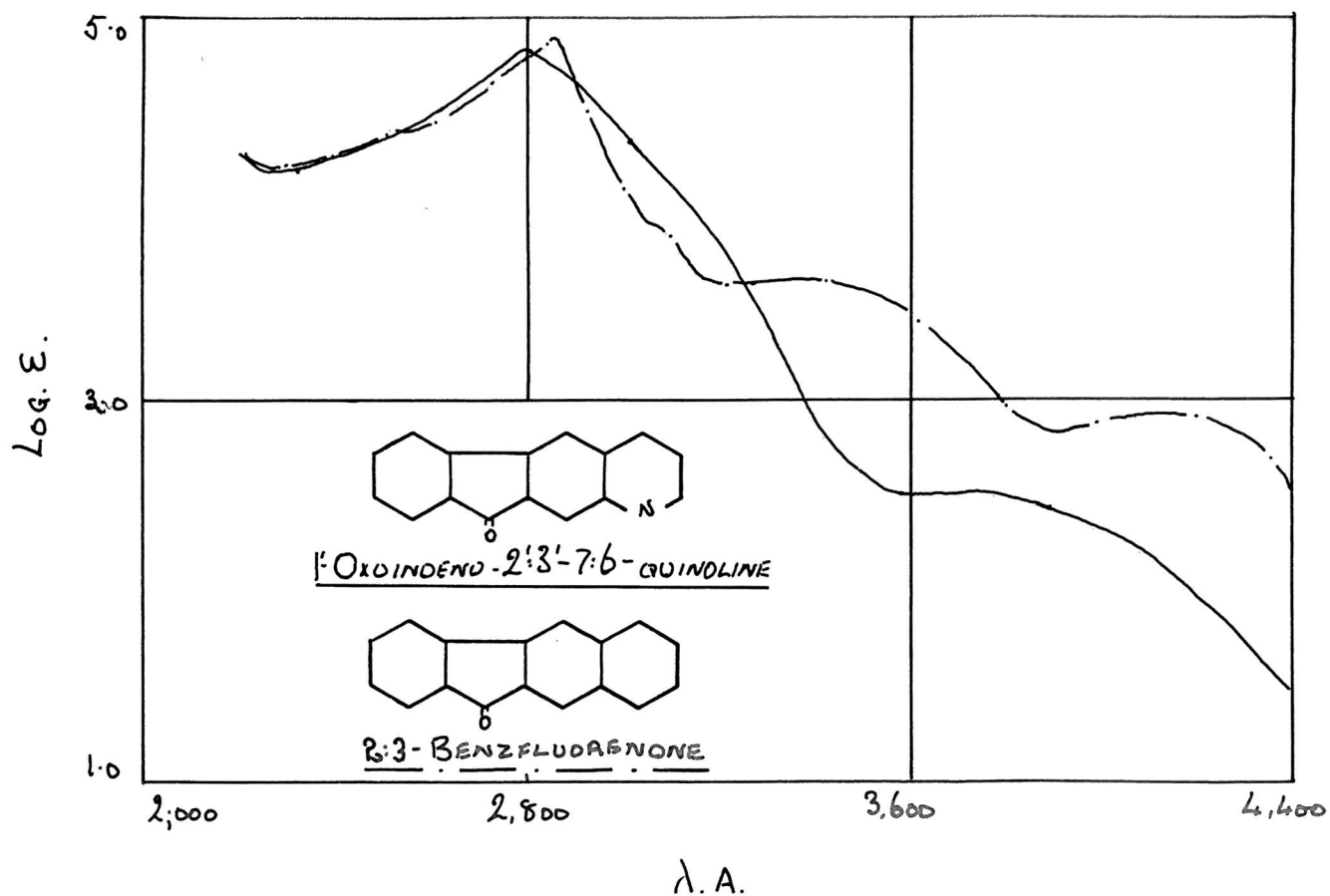
was dissolved in phosphorus oxychloride and boiled with phosphorus trichloride. On removing the solvent a dark sticky material was left which on treatment with sodium bicarbonate turned into a solid, resinous mass from which no crystalline solid could be obtained. It will be remembered that Clemo could not effect this change with 4-hydroxyindeno-2':3'-5:6-quinoline. Since the zinc dust distillation of 4-hydroxymethylindeno-2':3'-7:6-quinaldine had been so successful, this classical method was applied to this hydroxyindenoquinaldine. Unfortunately heating this substance with zinc only resulted in much charring, no product distilled out of the reaction mixture.

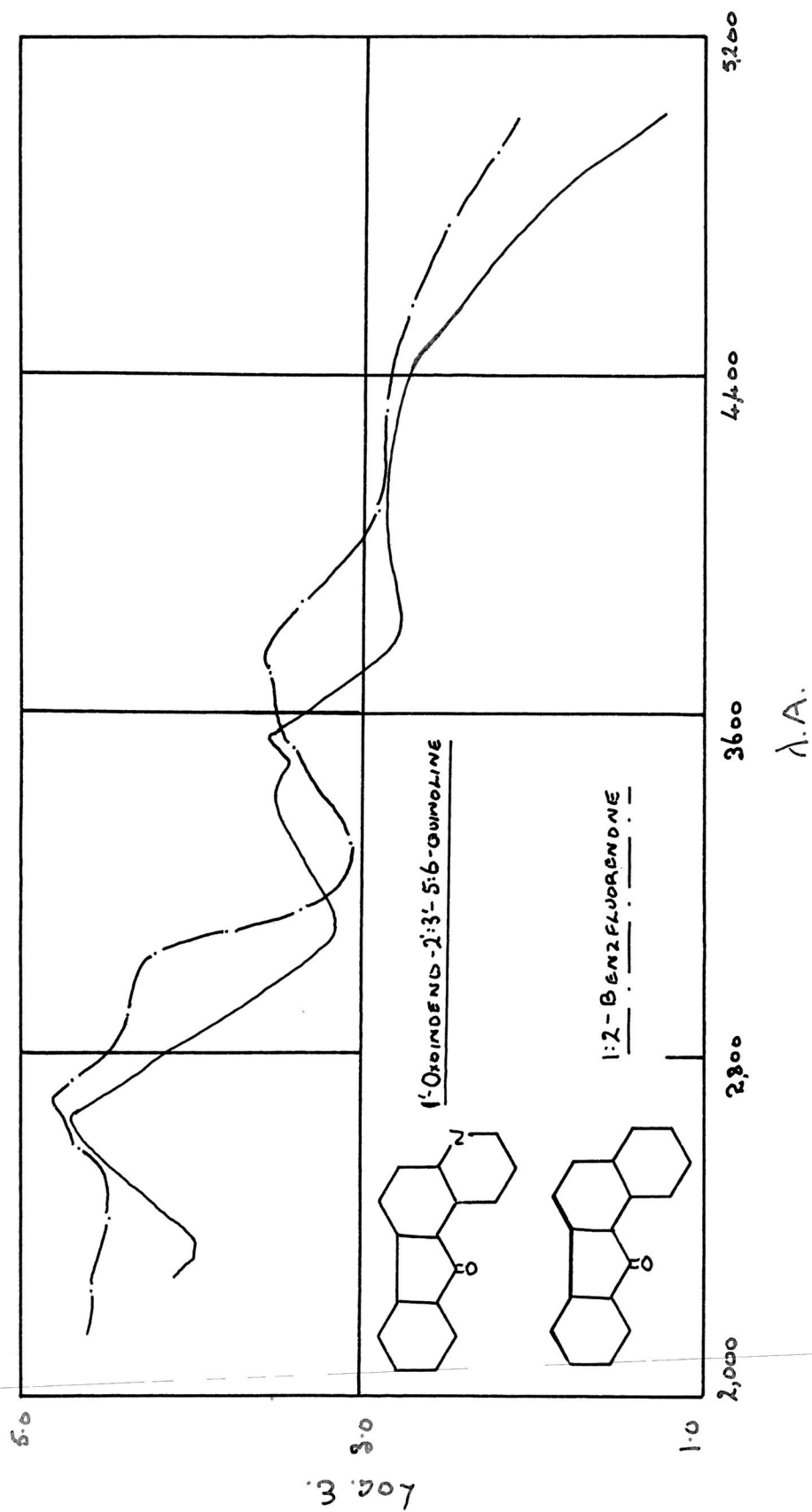
Hughes had also applied the Knorr reaction to 2-aminofluorene.



This reaction was carried out and an effort made to remove the hydroxyl group in this substance. Treatment with phosphorus trichloride yielded a tarry material from which no crystalline substance could be obtained. Zinc dust distillation was tried but again only charring took place. These experiments indicate/

indicate that some altogether different approach will have to be made in order to decide the structure of these two compounds.

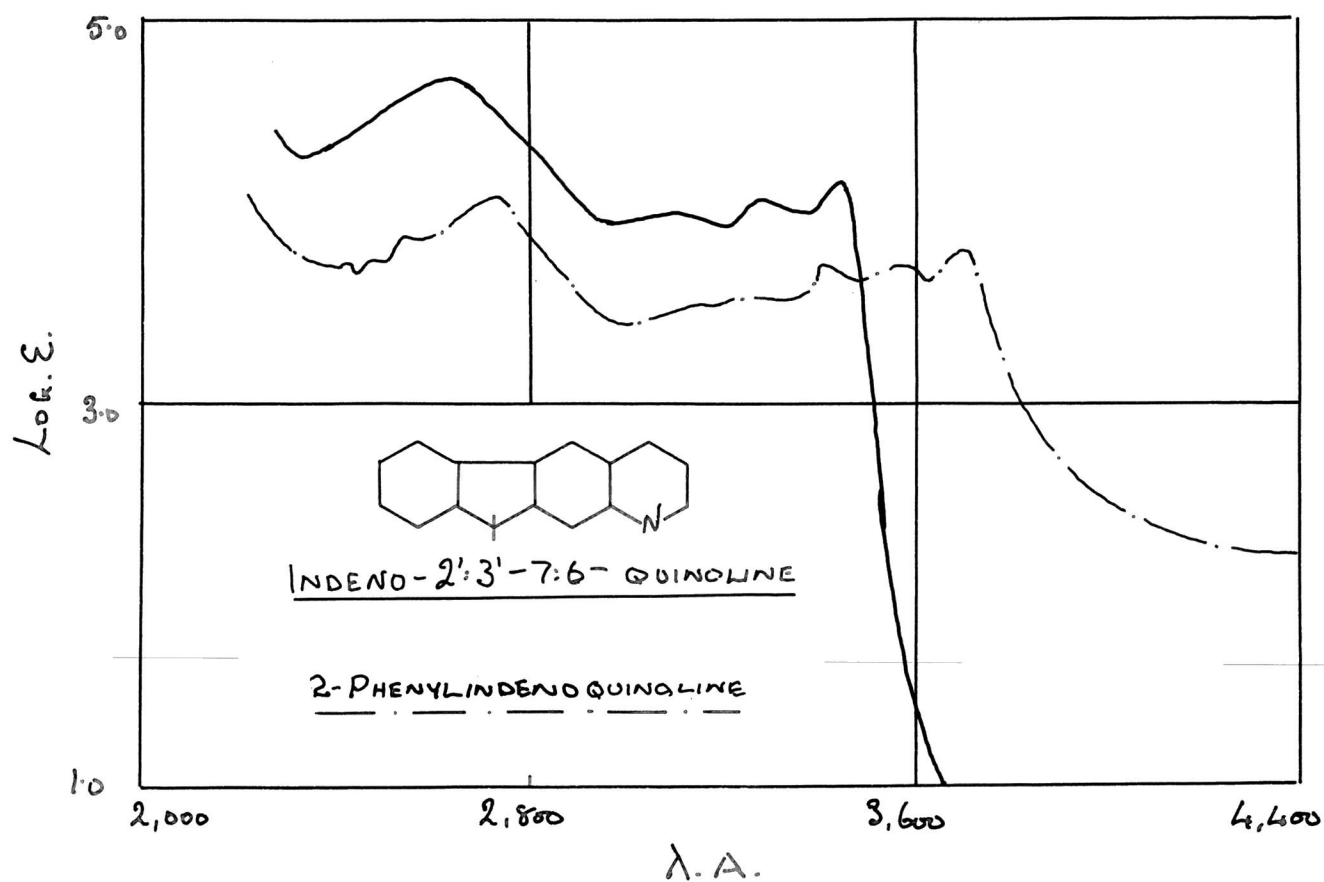
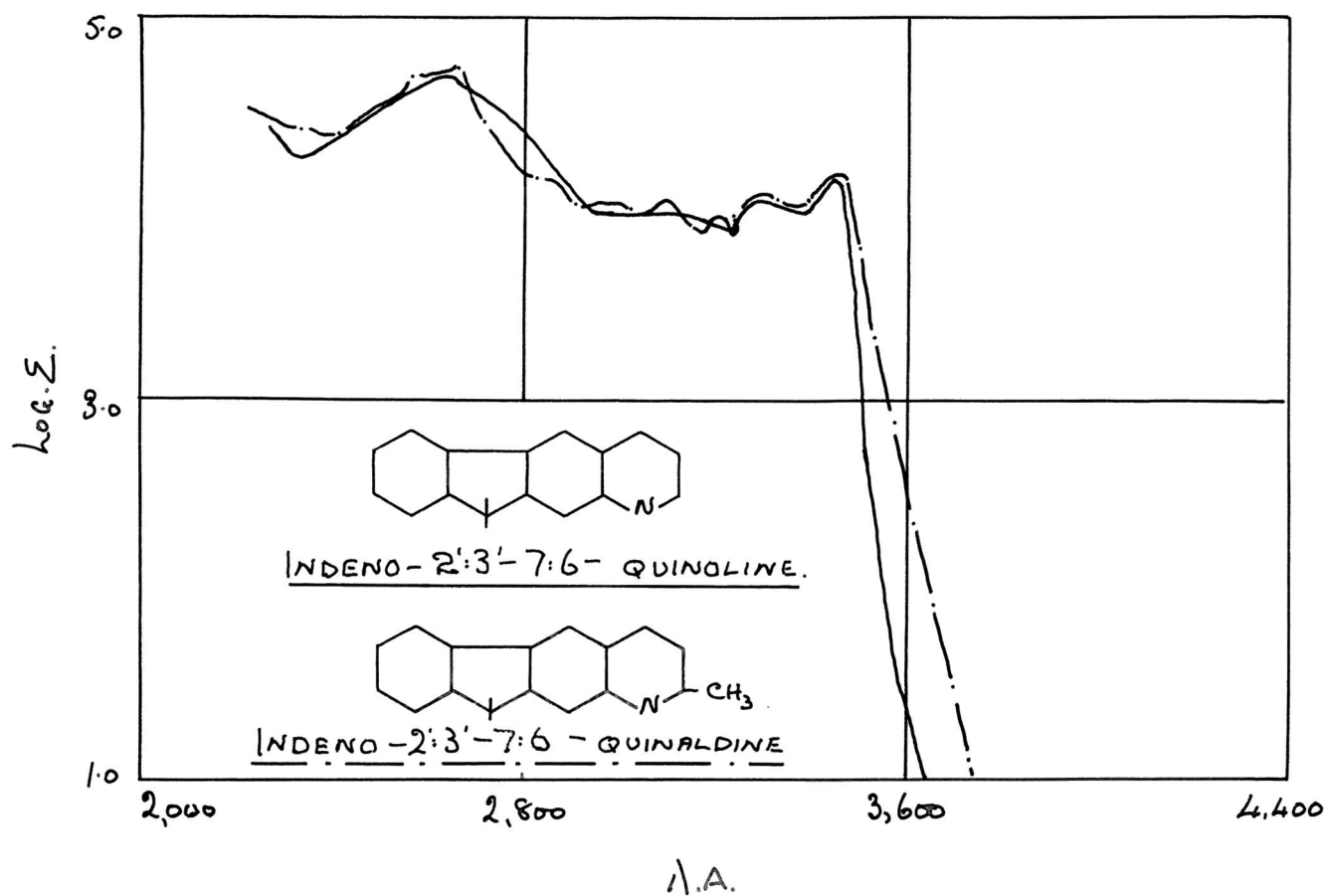




The Absorption Spectra of the "Diels Quinoline"
and Related Compounds

The absorption spectra of the "Diels quinoline" has been compared with that of 1:2-benzfluorene and 2:3-benzfluorene by Campbell and Stafford (4) and by Clemo (31). The absorption curves of the two hydrocarbons are very similar so that comparison of the absorption curve of the "Diels quinoline" with them provides doubtful evidence as to the structure of the quinoline. Nevertheless Campbell and Stafford suggested correctly, on this basis, the structure of the "Diels quinoline" to be indeno-2':3'-7:6-quinoline, while Clemo wrongly suggested the structure to be indeno-2':3'-5:6-quinoline.

The curves of the absorption spectra of 1:2- and 2:3-benzfluorenones show much greater differences than in the case of the corresponding benzfluorenes, so that in this work the absorption spectra of the two oxoindenoquinolines were measured and the absorption curves compared with those of the benzfluorenones (see opposite). As might be expected the product of oxidation of the "Diels quinoline" shows a great similarity to 2:3-benzfluorenone while 1'-oxoindeno-2':3'-5:6-quinoline is very similar to 1:2-benzfluorenone. This offers much better evidence as to the structure of the quinolines than the comparison made by Campbell and Stafford, and Clemo, and may be regarded as confirming the chemical evidence just described. The absorption curve of 1'/



1'-oxoindeno-2':3'-7:6-quinaldine is very like that of the 1'-oxoindeno-2':3'-7:6-quinoline, the methyl group causing a slight bathochromic shift and an increase in the fine structure.

The absorption curves of the "Diels quinoline," indeno-2':3'-7:6-quinaldine and 2'-phenylindeno-quinoline (structure not known) are shown opposite. As might be expected the curves of the quinoline and the quinaldine are very similar, the methyl group again causing a slight bathochromic shift and an increase in the fine structure. The absorption curve of the phenyl compound is completely different, however, from the "Diels quinoline." This is in accord with what has been found in other series of compounds where a phenyl group can be planar with the rest of an aromatic molecule. The increased conjugation causes large changes in the absorption spectra to take place over that of the parent substance (51). A comparison of the absorption curves of these three substances does not, therefore, provide any evidence for the structure of the phenylindeno-quinoline.



EXPERIMENTAL

2-Nitrofluorene.

The procedure is essentially that of Diels (loc. cit.). Fluorene (60 g.) was dissolved in glacial acetic acid (500 mls.) at 50°. Nitric acid (80 mls., d. 1.42) was added dropwise to this solution with mechanical stirring. The mixture was gradually heated to 80° and allowed to stand at this temperature for 10 minutes. On cooling, the solution deposited crystals of 2-nitrofluorene which were removed, washed with glacial acetic acid and then with much water. It is essential to wash free of nitric acid before attempting to recrystallise. The crude material was dried and recrystallised from glacial acetic acid yielding 2-nitrofluorene as pale yellow needles.

m.p. 157°, lit. m.p. 157°.

Yield 60 g., 80%.

2-Aminofluorene.

Finely reduced iron powder (10 g.) was added to a vigorously boiling suspension of 2-nitrofluorene (12.5 g.), in ethanol (180 mls.). Conc. hydrochloric acid (250 mls.) was added dropwise over a period of 1½ hours, and the solution boiled for a further 2 hours. The mixture was cooled in ice-water and filtered. The amine hydrochloride was washed with a little cold ethanol, transferred to a beaker, dissolved in water and basified. The free base contaminated with ferric hydroxide was filtered off and air dried. Recrystallisation from ethanol (charcoal)/

(charcoal) yielded 2-aminofluorene as almost colourless needles.

m.p. 125 - 126°, lit. m.p. 127°.

Yield 9.3 - 10.3 g., 89 - 96%.

Catalytic reduction of 2-nitrofluorene.

2-Nitrofluorene (5.0 g.) and Raney nickel (0.5 g.) were suspended in ethyl acetate (200 mls.) and hydrogenated at room temperature and at 60 lbs./sq. in. The solution was filtered, reduced to small bulk and allowed to stand. A buff coloured precipitate appeared which was removed and recrystallised from ethyl acetate/petrol to yield buff coloured needles.

m.p. 275 - 277°, lit. m.p. 2:2'-Azoxyfluorene 279°.

Yield 2.8 g., 82% theory.

Skraups synthesis with 2-aminofluorene - "Diels Quincline."

2-Aminofluorene (6.0 g.), glycerol (18 g.), arsenic pentoxide (9.2 g.) and conc. sulphuric acid (5.0 g.) were thoroughly mixed and then boiled gently under reflux for 5 hours. The reaction mixture was poured into ice-water (200 g.) and basified with 40% caustic soda. The resulting black flocculent precipitate was filtered off, air dried and finally dried at 80°. Soxhlet extraction with benzene gave a dark brown solution with a green fluorescence. The solution was reduced in bulk and chromatographed on alumina. A colourless band with a brilliant white fluorescence in U.V. light rapidly separated from the black material at the top of the column./

column. Elution of this band with benzene gave a colourless solution which deposited colourless plates on evaporation to small bulk. Recrystallisation was best accomplished from light petroleum (b.p. 60 - 80°) containing 10% benzene.

m.p. 133°, lit. m.p. 133°

Yield 4 - 4.5 g., 57 - 64%.

Reduction of "Diels Quinoline."

(a) Tin and HCl.

"Diels quinoline" (1.0 g.) was dissolved in conc. hydrochloric acid (20 mls.), and the mixture boiled for 2 hours with HCl. gas passing through the mixture. The hot solution was filtered and then chilled in ice-water; colourless crystals of the stannichloride separated (m.p. > 360°). This material was filtered off dissolved in caustic soda and extracted with ether. The ethereal solution was dried over anhydrous sodium sulphate and the ether removed. A brown oil was left which would not crystallise. This oil was dissolved in benzene and chromatographed on alumina (4" x $\frac{1}{2}$ "). A pale yellow band appeared which was eluted with benzene to give a yellow solution. Removal of the solvent gave back the oil. The oil was again dissolved in benzene (5 mls.) and a saturated solution of picric acid in benzene added; no picrate was obtained.

The experiment was repeated doubling the reaction time. The product was again an oil which would not crystallise.

(b)/

(b) Sodium and amyl alcohol.

"Diels quinoline" (1.0 g.) was dissolved in amyl alcohol (25 mls.), sodium (1.3 g.) was added to the boiling solution, in small pellets over a period of 1 hour. Boiling was continued until all the sodium had dissolved. The solvent was removed under reduced pressure leaving a sticky mass of alkoxide and product. This was dissolved in water and extracted with ether (2 x 100 mls.). The etherial solution was washed well with water, dried over anhydrous sodium sulphate and then distilled to dryness. An oil was obtained having properties similar to that described above.

(c) Sodium and ethanol.

"Diels quinoline" (1.0 g.) was dissolved in ethanol (25 mls.), sodium (1.3 g.) was added in small pellets to the boiling solution over a period of 1 hour. The reaction mixture was worked up as above, again yielding an intractible oil.

Attempted ring fission of "Diels quinoline."

(a) "Diels quinoline" (2.0 g.) was shaken with a mixture of benzoyl chloride (2.5 mls.) and aqueous caustic soda (12 mls., 10%) for 12 hours. Starting material was recovered quantitatively.

(b) "Diels quinoline" (2.0 g.) was dissolved in dioxan (30 mls.). This solution was added to benzoyl chloride in aqueous caustic soda (12 mls., 10%) and the whole shaken for 2 hours. The solution was poured into benzene (100 mls.), washed with water/

water (3 x 50 mls.) and dried over anhydrous sodium sulphate. Removal of the solvent yielded starting material (90% recovery).

4- and 6-Nitro-m-toluidine.

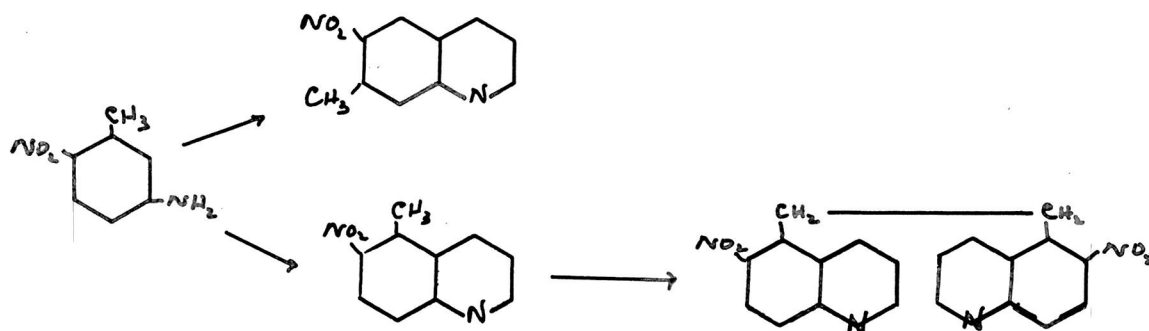
m-Acetotoluidide (25 g.) was added in 2 g. quantities to a mixture of acetic acid (100 mls.), conc. sulphuric acid (60 mls.) and nitric acid (d. 1.47, 68 mls.) over a period of 1 hour. Throughout the addition the solution was mechanically stirred and maintained at 15°. The mixture was poured into brine-ice (1 L.), the precipitate removed and air dried.

The crude mixture of nitro-acetotoluidides was hydrolysed by boiling with sulphuric acid (70%, 170 mls.) for 1 hour after which it was poured into ice-water and basified. The precipitate was removed, air dried and finally dried on porous plate. The mixture can be separated by fractional crystallisation from carbon tetrachloride in which 4-nitro-m-toluidine is more soluble. Crystallisation from benzene was found to be just as effective and from this solvent pure 6-nitro-m-toluidine was obtained as large, bright yellow needles.

m.p. 133 - 4°, lit. m.p. 134°.

Yield 22 g., 66%.

6-Nitro-7-methylquinoline./

6-Nitro-7-methylquinoline.

6-Nitro-m-toluidine (30 g.), glycerol (65 g.), conc. sulphuric acid (60 g.), and arsenic pentoxide (32 g.) were gently boiled under reflux for $2\frac{1}{2}$ hours. The reaction mixture was poured into water and basified with caustic soda. The precipitate was removed, dissolved in hydrochloric acid (500 mls., 50%) and boiled with decolourising charcoal. The mixture of quinoline was precipitated as a dirty grey sludge by basifying the acid solution with caustic soda. This material was removed, dried and dissolved in benzene. The resulting solution was chromatographed on alumina (8" x $1\frac{1}{2}$ "). A colourless band (white in U.V. light) rapidly separated from the black band at the top of the column, and was eluted with benzene. The eluate on concentration deposited long colourless needles, m.p. $118 - 119^{\circ}$, yield 32.5 g. This material appeared to be mixed crystals of the two isomers, for by chromatographing 1.0 g. in benzene/petrol separation into the two isomers was achieved.

Separation/

Separation on the large scale was best accomplished by making use of the fact that 6-nitro-5-methylquinoline on boiling in alcoholic sodium hydroxide reacts to give a dinitrodiquinolylethane, while 6-nitro-7-methylquinoline does not react.

The crude mixture of quinolines (30 g.) was dissolved in methanol (500 mls.) and sodium hydroxide (12 g.) in water (30 mls.), added. The mixture was boiled for 1 hour, chilled and filtered to remove the diquinolylethane. The filtrate was evaporated to dryness and the residue dissolved in benzene. The benzene solution was chromatographed on alumina to separate the 6-nitro-7-methylquinoline from resinous material which appeared during the reaction. 6-Nitro-7-methylquinoline was obtained as colourless needles.

m.p. 140° , lit. m.p. 140° .

Yield 16.2 g., 43%.

Attempted oxidation of 6-nitro-7-methylquinoline.

6-Nitro-7-methylquinoline (1.0 g.) was dissolved in glacial acetic acid (7 mls.) and chromic oxide (1.0 g.) in water (2 mls.) added. The solution was boiled for 2 hours after which the solvent was removed under reduced pressure. The green sticky mass was taken up in water, made slightly acid with dilute acetic acid and extracted with ether. The etherial solution was washed well with water and then dried over anhydrous sodium sulphate. Removal of the solvent yielded no 6-nitroquinoline-7-carboxylic acid./

acid. Basifying the aqueous solution yielded no starting material.

This experiment was repeated several times varying the time of boiling and using sodium dichromate in place of chromic oxide. In no case was any acidic material isolated.

The oxidation was then attempted with dilute nitric acid in a sealed tube. 6-Nitro-7-methylquinoline (1.0 g.) was dissolved in nitric acid (15 mls., d. 1.20) in a Carius tube and heated for 12 hours at 150°. On cooling the tube a crystalline substance was deposited which proved to be the nitrate of the base from which starting material was recovered almost quantitatively.

The reaction was repeated this time heating for 12 hours at 220°. On opening, the tube was found to contain a large quantity of gas. Working up the solution yielded a 20% recovery of starting material.

Bromination of 6-nitro-7-methylquinoline.

6-Nitro-7-methylquinoline (1.0 g.) and anhydrous sodium acetate (5.0 g.) were dissolved in glacial acetic acid (25 mls.), to this solution was added bromine (3.0 g.) in glacial acetic acid (25 mls.). The solution was boiled for 2 hours during which time sodium bromide precipitated out. The solution was filtered and evaporated to small bulk. On pouring into water a cream coloured precipitate was thrown down which was filtered off and dried. This substance was recrystallised many times from benzene to/

to give buff needles, m.p. 204 - 214°. This melting point could not be improved by recrystallisation.

$C_{10}H_5N_2O_2Br_3$ requires Br 56.5%.

$C_{10}H_6N_2O_2Br_2$ requires Br 45.2%.

found Br 46.3%.

Attempted hydrolysis of above dibromo-compound.

The dibromo-compound (1.0 g.) was refluxed with 10% sulphuric acid in which it was sparingly soluble. After boiling for 4 hours very little change appeared to have taken place. The solution was cooled, the solid removed and triturated with carbonate. Starting material was obtained almost quantitatively.

The experiment was repeated using more concentrated sulphuric acid (60%) but again no hydrolysis took place. Boiling with caustic soda solution (10%) gave a sticky, tarry substance from which no crystalline substance could be isolated.

7- and 3-Nitro-2-aminofluorene.

Nitric acid (5 mls., d. 1.5) was added with mechanical stirring over a period of 5 minutes to 2-acetamidofluorene (10 g.) dissolved in acetic acid (100 mls.) at 50°. After standing at this temperature for 30 minutes the solution was poured onto crushed ice (500 g.). The precipitate was filtered, washed free of acid, and air dried. The crude mixture was hydrolysed by boiling for 1 hour with hydrochloric acid (18 mls. conc.) in ethanol (360 mls.). The mixture was reduced in volume to 120 mls. and allowed to stand for 2 hours. The red solid/

solid which separated was filtered off and boiled in dilute hydrochloric acid (400 mls. conc. in 800 mls. water) for 1 hour. The cold mixture was filtered. The residue was re-extracted - 7 times in all - yielding moderately pure 3-nitro-2-aminofluorene. Basification of the filtrates yielded 7-nitro-2-aminofluorene. The 3-nitro-2-aminofluorene was finally purified by chromatographing on alumina (9" x $\frac{1}{2}$ ") in pure xylene. The amine crystallised from xylene or dilute acetic acid in crimson needles.

m.p. 202 - 203°, lit. m.p. 203°.

Yield 4.1 g., 37%.

Skraups synthesis with 3-nitro-2-aminofluorene.

3-Nitro-2-aminofluorene (2.0 g.), anhydrous glycerol (9.0 g.), arsenic pentoxide (4.6 g.) and conc. sulphuric acid (2.0 g.) were heated together for 5 hours. The reaction mixture was poured into ice-water (100 g.) and basified. The precipitated tarry material was filtered off and dried in a vacuum desiccator over phosphorus pentoxide. Soxhlet extraction of this material for 3 hours with benzene yielded a dark solution with a green fluorescence. This solution was evaporated to small bulk (about 25 mls.) and chromatographed on alumina; benzene quickly developed a yellow band which on elution yielded a pale yellow solution. On reduction to small bulk this solution deposited pale yellow needles which were recrystallised from ethanol.

m.p./

m.p. 187 - 189°.

Yield 6.612 g., 2%.

$C_{16}H_{10}N_2O_2$ requires C 73.3%, H 3.8%, N 10.7%.

$C_{16}H_9NO$ requires C 83.1%, H 3.9%, N 6.1%.

found C 82.9%, H 4.3%, N 5.6%.

The analysis of this compound approximates to that of an oxoindenoquinoline. This substance did not depress the melting point of the product of oxidation of "Diels quinoline."

Attempted debromination of 2-bromofluorene.

2-Bromofluorene (1.0 g.), hydriodic acid (7 mls., d. 1.94) and red phosphorus (0.2 g.) were boiled together for 4 hours. The reaction mixture was poured into potassium iodide solution (100 mls., 2%) and the precipitated product filtered off. Recrystallisation from alcohol after hot filtering yielded starting material almost quantitatively.

Attempted debromination of 2:7-dibromofluorene.

2:7-Dibromofluorene (0.5 g.) hydriodic acid (7 mls., d. 1.94) and red phosphorus (0.2 g.) were boiled together for 4 hours. Working up as in the last experiment yielded an almost quantitative return of starting material.

Debromination of 2:3:7-tribromofluorenone.

2:3:7-Tribromofluorenone (1.0 g.), hydriodic acid (7.5 mls., d. 1.94) and red phosphorus (0.2 g.) were boiled together for 4 hours. The reaction product was poured into potassium iodide solution (100 mls., 2%), and filtered. The residue was recrystallised/

crystallised from acetic acid (Charcoal).

m.p. 162° , lit. m.p. of 2:7-dibromofluorenone
 162° .

mixed m.p. 162° .

Yield 0.6 g., 85%.

Debromination of 3:7-dibromo-2-aminofluorene.

3:7-Dibromo-2-aminofluorene (1.0 g.) was boiled with red phosphorus (0.2 g.) in hydriodic acid (7.5 mls., d. 1.94) for 4 hours. The reaction mixture was worked up as above, the product dissolved in acetic acid (charcoal), and then boiled with a little acetic anhydride. The amine was isolated as its acetyl derivative.

m.p. 231° , lit. m.p. of 7-bromo-2-acetamidofluorene 231° .

mixed m.p. 231° .

Yield 0.65 g., 85%.

3:7-Dibromo-2-p-toluenesulphonamidofluorene.

Prepared according to Bell and Mulholland, J., 1949, 2021.

3:7-Dibromo-2-aminofluorene.

The above compound could not be obtained by hydrolysis of its tosyl derivative. This reaction was attempted in several ways, by standing in cold conc. sulphuric acid, by boiling with 70% sulphuric acid and by boiling with 10% NaOH. In each case only a negligible quantity of the amine was obtained. Warming with conc. sulphuric acid resulted in much charring.

2-Bromofluorene./

2-Bromofluorene.

Prepared according to Gilmore (Thesis - Edinburgh).

7-Bromo-2-nitrofluorene.

2-Bromofluorene (60 g.) was dissolved in the minimum of glacial acetic acid at 50° (approx. 500 mls.). Nitric acid (50 mls., d. 1.42) was added over a period of 15 minutes with mechanical stirring, and a little yellow precipitate appeared. The temperature was gradually raised to 80° and kept at this for 5 minutes. In order to prevent further nitration the temperature was not allowed to rise above 80°. The mixture was allowed to cool slowly to room temperature.

The precipitate was filtered off, washed with a little glacial acetic acid and then with a large volume of water. One recrystallisation from glacial acetic acid was sufficient to yield pure 7-bromo-2-nitrofluorene.

m.p. 236°, lit. m.p. 236°.

Yield 55 g., 67%.

A small amount of 2:7-dibromofluorene was obtained from the reaction mother liquors.

7-Bromo-2-aminofluorene.

Conc. hydrochloric acid (200 mls.) was added dropwise over a period of 2 hours to a mixture of 7-bromo-2-nitrofluorene (25 g.) and finely reduced iron powder (30 g.), suspended in boiling ethanol (600 mls.). During the addition of the acid a colourless/

colourless crystalline precipitate of amine hydrochloride appeared.

The mixture was chilled in ice-water and filtered to remove the amine hydrochloride which was washed on the filter with a little ice cold hydrochloric acid. The free amine, contaminated with ferric hydroxide, was liberated by suspending the precipitate in water and adding caustic soda. The amine was recrystallised from aqueous ethanol (charcoal). 7-Bromo-2-aminofluorene was obtained in buff coloured needles.

m.p. $140 - 141^{\circ}$, lit. m.p. 142° .

Yield 22 g., 90%.

7-Bromo-2-acetamidofluorene.

7-Bromo-2-aminofluorene (20 g.) was dissolved in the minimum of boiling acetic acid and acetic anhydride (20 mls.) added. The mixture was boiled for 10 minutes and then distilled down to $\frac{1}{3}$ bulk; hot water was added in excess. After cooling the precipitate was removed and recrystallised from acetic acid to yield colourless needles.

m.p. $230 - 231^{\circ}$, - lit. m.p. 232° .

Yield 18.4 g., 81%.

3:7-Dibromo-2-acetamidofluorene.

7-Bromo-2-acetamidofluorene, (10 g.) was dissolved in nitrobenzene (45 mls.) at 45° . Bromine (7 g.) was added and the mixture allowed to stand at room temperature for 3 hours. The nitrobenzene was removed by distilling in steam superheated to 150° .

The/

The residue was recrystallised from acetic acid to yield straw coloured needles.

m.p. $270 - 2^{\circ}$, lit. m.p. 272° .

Yield 10 g., 80% theory.

3:7-Dibromo-2-aminofluorene.

3:7-Dibromo-2-acetamidofluorene (10 g.), sulphuric acid (100 mls., 70%) and glacial acetic acid (50 mls.) were refluxed together for $1\frac{1}{2}$ hours. The mixture was poured onto crushed ice (150 g.), basified with ammonia, and the solid removed. Recrystallisation from acetic acid yielded a buff coloured powder (micro-crystalline).

m.p. $133 - 134^{\circ}$, lit. m.p. 134° (145°).

Yield 10 g., 80% theory.

Skraup's synthesis with 3:7-dibromo-2-aminofluorene.

3:7-Dibromo-2-aminofluorene (3 g.), glycerol (4.8 g.), arsenic pentoxide (2.4 g.) and conc. sulphuric acid (3.0 g.) were boiled together gently, on an oil bath, for 6 hours.

The reaction mixture was poured into water, basified with caustic soda (40%) and the dark tarry precipitate removed and dried as far as possible on the filter. Water was removed completely by azeotropic distillation with benzene. The benzene solution (about 250 mls.) was filtered and chromatographed on alumina ($5'' \times \frac{3}{4}''$). A colourless band with a brilliant white fluorescence in the U.V., separated slowly from the black band at the top of the column. Elution of this band yielded a compound/

compound crystallising in colourless needles from benzene.

m.p. $200 - 201^{\circ}$, - lit. m.p. 210° .

Yield 0.010 g.

$C_{16}H_9NBr_2$ requires Br 42.7%.

found Br 41.7%.

The chromatographic column was then extruded; the black portion at the top rejected, and the remainder extracted (Soxhlet) with methanol in an attempt to recover any quinoline left on the column; none was recovered.

The black insoluble residue from the original benzene liquors was then extracted with HCl (100 mls., 50%) to remove any basic material. Evaporation of the solution to $\frac{1}{4}$ bulk followed by basification yielded no organic material.

This experiment was repeated with the same yield.

4-Nitrofluoranthene.

Fluoranthene (30 g.) was dissolved in the minimum of glacial acetic acid at 30° (approx. 1.2 L.). Nitric acid (150 mls., d. 1.51) was added dropwise to the stirred solution, the temperature increasing from $30 - 35^{\circ}$. The mixture was stirred for 4 hours, a yellow-orange precipitate appearing. This material was filtered off, washed with a little cold acetic acid, with water and finally dried at 100° . Four recrystallisations from glacial acetic acid yielded pure 4-Nitrofluoranthene.

m.p./

m.p. 159° , lit. m.p. 160° .

Yield 7.8 g., 21%.

4-Acetamidofluoranthene.

4-Nitrofluoranthene (5.0 g.) was suspended in acetic acid (200 mls., A.R.) and Raney nickel (0.1 g.) added. The mixture was hydrogenated at 3 atmospheres pressure. When the uptake of hydrogen had ceased, the solution was filtered and concentrated to 50 mls. Acetic anhydride (10 mls.) was added to the solution which was then boiled for 10 minutes, water was added until a faint precipitate appeared and the solution then set aside to cool. The acetyl compound crystallised in colourless needles.

m.p. 240° - 242° , lit. m.p. 240° .

Yield 4.7 g., 85%.

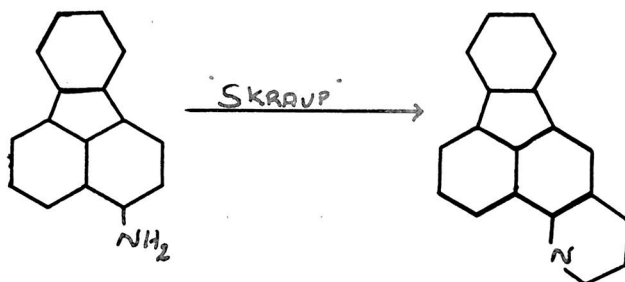
4-Aminofluoranthene.

4-Acetamidofluoranthene (5.0 g.) was boiled with sulphuric acid (50 mls., 60%) for 1 hour. The solution was basified and extracted with ether (2 x 200 mls.); the ether extract was dried over anhydrous sodium sulphate. Removal of the solvent yielded a green, highly fluorescent oil which solidified on cooling. The amine can be recrystallised from aqueous ethanol.

m.p. 109 - 111° , lit. m.p. 111 - 112° .

Yield 4.2 g., 92%.

Skraup's synthesis with 4-aminofluoranthene -
pyrido-2':3'-4:3-fluoranthene.



4-Aminofluoranthene (3.0 g.), glycerol (12.6 g.), conc. sulphuric acid (4.0 g.) and arsenic oxide (6.4 g.) were heated together for a period of 6 hours. The reaction mixture was poured into water, basified and the precipitate extracted with ether (2 x 100 mls.). The ether was removed and the residue dissolved in benzene and chromatographed on alumina (2" x $\frac{1}{2}$ ") to yield a colourless solution which on evaporation deposited pale yellow prisms. This material was recrystallised from alcohol, from which it crystallised in needles.

m.p. 169 - 170°.

Yield 0.4 g., 12%.

C₁₉H₁₁N requires C 90.1%, H 4.4%, N 5.5%.

found C 90.2%, H 4.3%, N 5.8%.

Acetylation of phenanthrene.

Carried out according to the directions of Mossetig and Kruger, J.A.C.S., 1930, 52, 3704.

2-Acetamidophenanthrene.

2-Acetylphenanthrene (2.2 g.) was dissolved in trichloroacetic acid (15 g.) at 60° (oil bath temperature), sodium azide (1.0 g.) was added and the solution/

solution heated for 4 hours. A further quantity of sodium azide (0.2 g.) was added and heating continued for 3 more hours. Throughout the period of heating the mixture was occasionally shaken. The reaction mixture was poured onto crushed ice (50 g.) and the precipitate removed by filtration. Recrystallisation (charcoal) from ethanol yielded pure 2-acetamidophenanthrene as short colourless needles.

m.p. 225° , lit. m.p. $225 - 226^{\circ}$.

Yield 1.7 g., 72%.

The experiment was repeated on a five fold scale.

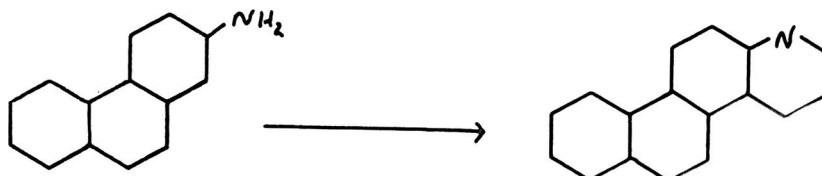
2-Aminophenanthrene.

2-Acetamidophenanthrene (1.7 g.) was dissolved in methanol (100 mls.) containing conc. hydrochloric acid (15 mls.). The mixture was boiled for 5 hours and the amine hydrochloride separated out. This substance was filtered off, dissolved in water, basified and extracted with ether; after drying over anhydrous sodium sulphate the ether was removed completely and the residue recrystallised from methanol to yield 2-aminophenanthrene as buff coloured needles.

m.p. $83 - 88^{\circ}$, lit. m.p. 85° .

Yield 1.3 g., 92%.

3-Azachrysene.



The method of Mossetig and Kruger was employed.
The following was preferred.

2-Aminophenanthrene (5.0 g.), glycerol (11 g.),
conc. sulphuric acid (7 mls.) and arsenic pentoxide
(9.0 g.) were boiled together for 4 hours. The re-
action product was poured into water, the dark floc-
culent precipitate removed and boiled with HCl
(charcoal). Basification of this acid solution
yielded a grey precipitate which was recrystallised
to purity from toluene.

m.p. 129 - 130°, lit. m.p. 129 - 130°.

Yield 4.2 g., 69%.

3-Azachrysene-7:8-quinone.

3-Azachrysene (0.1 g.) was dissolved in glacial
acetic acid (5 mls., A.R.) and chromic oxide (0.1 g.)
in water (1 ml.) added. On adding the chromic
oxide a precipitate appeared which dissolved on boil-
ing (2 - 3 minutes). The solvent was then removed
under vacuum and the residue extracted with water.
The water insoluble material was removed, dried and
recrystallised from xylene/petrol or sublimed (190°
at 0.01 m.m. Hg.) to give crimson needles.

m.p. 285 - 6°.

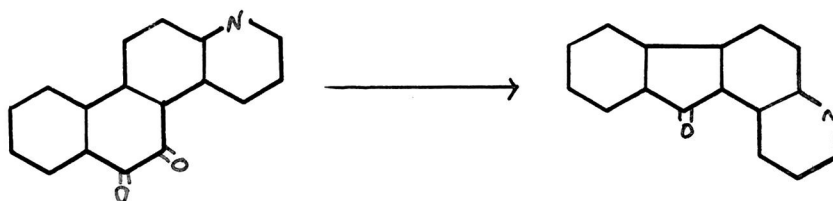
Yield 11 m.g., 10%.

The analysis showed that this substance was not
absolutely pure but indicated that it was essentially
the correct compound. It was not found possible to
purify this compound completely.

In another experiment, 3-azachrysene (0.2 g.)
was/

was shaken in the cold for 36 hours with chromic oxide (1.1 g.) in glacial acetic acid (10 mls., A.R.). On removing the solvent and pouring into water, no precipitate appeared. The solution was extracted at pH 2 with ether giving a small amount of a colourless substance m.p. $200 - 202^{\circ}$ in insufficient quantity for analysis. No starting material could be recovered.

1'-Oxoindeno-2':3'-5:6-quinoline.



3-Azachrysene-7:8-quinone (0.020 g.) was suspended in aqueous caustic potash (6 mls., 5%) containing methanol (3 mls.) and heated on a boiling water bath for 36 hours. Throughout the time of heating a stream of air was blown through the reaction mixture. The crimson quinone needles were gradually replaced by golden yellow needles. The solution was evaporated to half bulk under vacuum and the yellow material removed by filtration. This substance was recrystallised from ethanol.

m.p. $173 - 179^{\circ}$.

Yield 0.009 g., 50%.

$C_{16}H_9N$ O requires C 83.1%, H 3.9%, N 6.1%.

found C 83.2%, H 4.1%, N 5.8%.

A mixture of this substance and the ketone (m.p. 190°)/

(m.p. 190°) obtained by oxidising "Diels quinoline" showed a very great depression in melting point.

Oxidation of "Diels quinoline."

"Diels quinoline" (5.0 g.) was boiled in acetic acid (50 mls.) with sodium dichromate (17 g.) for 2 hours. The solution was distilled to half bulk and poured into water. The precipitate was removed and triturated with caustic soda, filtered, and washed well with water. This material was recrystallised from methanol (charcoal) to yield the oxoindeno-quinoline as lemon-yellow needles.

m.p. 190° , lit. m.p. 190° .

Yield 3.5 g., 65%.

Ring opening of 1'-oxoindeno-2':3'-7:6-quinoline and cyclisation of resulting acid to give 1'-oxoindeno-2':3'-5:6-quinoline.

1'-Oxoindeno-2':3'-7:6-quinoline (1.0 g.) was added in small portions to a mechanically stirred mixture of potassium hydroxide (3 g.) and diphenyl ether (30 mls.) at 180° , and kept at this temperature for 2 hours. The mixture was poured into benzene and the precipitated potassium salt of the acid removed.

The potassium salt was added to cold, conc. sulphuric acid (3 mls.) and then heated for 1 hour at 100° . The solution developed a deep violet colour after 30 minutes heating. Pouring into water and basifying gave a yellow precipitate which was removed and dried. The product was recrystallised from ethanol (charcoal) giving golden yellow needles. This substance, m.p. $178 - 179^{\circ}$, considerably depressed/

depressed the melting point of the starting material and did not depress the melting point of the benzilic acid rearrangement product of the azachrysenequinone.

Yield 0.47 g., 47%.

Indeno-2':3'-5:6-quinoline.

1'-Oxoindeno-2':3'-5:6-quinoline (0.20 g.) was dissolved in trimethylene glycol (10 mls.) containing hydrazine hydrate (0.5 mls., 90%), and caustic soda (0.1 g.). The mixture was boiled for 2 hours and a red precipitate appeared. The reflux condenser was removed and the temperature of the mixture allowed to reach 205° when the condenser was replaced and boiling continued for a further 2 hours. The solution was vacuum distilled to small bulk, poured into water and extracted with ether. The ether extract was dried over anhydrous sodium sulphate and then distilled to dryness leaving a small amount of oil. This oil was taken up in benzene and a saturated solution of picric acid (boiling) added. The picrate of the base precipitated and was filtered and dried. The picrate was added to a separating funnel containing benzene/ aqueous caustic soda. The free base dissolved in the benzene, which was then removed, washed with water, dried over anhydrous sodium sulphate, reduced to small volume and chromatographed on alumina. A colourless band which fluoresced white in U.V. light, developed, and was eluted with benzene. The benzene solution deposited colourless needles on evaporation to small bulk. This substance was recrystallised from benzene/

benzene/petrol. mp.?

$C_{16}H_{11}N$ requires C 88.5%, H 5.1%, N 6.4%.

found C 88.5%, H 5.2%, N 6.0%.

Doebner pyruvic acid synthesis with 2-aminofluorene +
indeno-2':3'-7:6-quinaldine-4-carboxylic acid.

The method of Neish loc. cit. was used.

It was found essential to use freshly distilled pyruvic acid in this experiment.

Yield 2.0 g., (from 3.0 g., 2-aminofluorene).

m.p. 350 - 355°, lit. m.p. 354 - 355°.

Esterification of above acid.

(1) The acid (1.0 g.) methyl alcohol (25 mls.) and conc. sulphuric acid were boiled together for 2 hours. The solution was then reduced to half bulk, poured into water, basified and extracted with ether (3 x 50 mls.). The ether solution was dried over anhydrous sodium sulphate, evaporated to dryness and the residue recrystallised several times from methanol.

m.p. 168 - 170°.

Yield 0.3 g., 28%.

$C_{19}H_{15}NO_2$ requires C 78.9%, H 5.2%, N 4.8%.

found C 78.3%, H 5.3%, N 4.9%.

(2) The experiment was repeated by suspending the acid (1.0 g.) in methanol (25 mls.) and bubbling HCl gas through the boiling mixture. The reaction mixture was worked up as above.

m.p. 168 - 170°.

Yield 0.50 g., 45%.

(3)/

(3) The best yields of the ester were obtained with diazomethane. The acid (1.0 g.) was suspended in dioxan (50 mls.), diazomethane (1.0 g.) in ether (100 mls.) was added with mechanical stirring. The mixture was allowed to stand overnight. The ether and dioxan were removed under reduced pressure, and the residue was recrystallised from methanol (charcoal) to yield the ester as colourless needles.

m.p. 168 - 170°.

Yield 0.80 g., 76%.

Attempted oxidation of indeno-2':3'-7:6-quinaldine-4-carboxylic acid to 1'-oxoindeno-2':3'-7:6-quinaldine-4-carboxylic acid.

The acid (0.5 g.) was suspended in glacial acetic acid (150 mls.) which had been purified by distillation from potassium permanganate. Sodium dichromate (1.5 g.) in acetic acid (10 mls.) was added to the above suspension and the whole boiled for 2 hours. The solution, which was now green, was evaporated to small bulk and poured into water. The brown precipitate was removed and dried. No solvent could be found which would recrystallise this material satisfactorily. Melting point determination indicated this to be mainly starting material.

The above experiment was repeated this time boiling for 24 hours. The product was worked up as before. Partial purification was affected by sublimation at $\frac{1}{2}$ m.m. pressure and 250°. The final product, which was not pure (m.p. 290 - 310°) was not investigated further.

Doebners/

Doebners pyruvic acid synthesis with 2-amino-9-fluorenol-1'-hydroxyindeno-2':3'-7:6-quinaldine-4-carboxylic acid.

2-Amino-9-fluorenol (3.0 g.) was dissolved in the minimum of boiling ethanol; pyruvic acid (3 mls.) was added to this solution which was then boiled for 6 hours. The precipitate which formed was removed, washed with ethanol and then ether. Recrystallisation of this substance was attempted from nitrobenzene and o-dichlorobenzene without success. No means of purifying this acid was found.

m.p. 300 - 310°.

Yield 1.90 g., 40%.

Esterification of above acid.

The acid (1.0 g.) was dissolved in methanol (50 mls.) containing conc. sulphuric acid (7 mls.) and boiled for 2 hours. On working up in the usual way a yellow solid was obtained which gave the ester as pale yellow needles after recrystallisation from benzene.

m.p. 227 - 228°.

Yield 0.52 g.

$C_{19}H_{15}N O_3$ requires C 74.7%, H 5.0%, N 4.6%.

found C 74.0%, H 5.0%, N 5.1%.

Decarboxylation of 1'-hydroxyindeno-2':3'-7:6-quinaldine-4-carboxylic acid with copper and quinoline.

The acid (1.0 g.) and copper-bronze powder (0.01 g.) were boiled together in quinoline (10 mls.) for 2 hours. The quinoline was removed by steam distillation, and the black residue dissolved in benzene. This solution was dried by distilling down to small bulk, and was then/

then chromatographed on alumina. On development with benzene, a yellow band quickly separated from the black band at the top of the column, and was eluted to give a pale yellow solution. This solution deposited yellow, needle shaped crystals which were recrystallised from benzene/light petroleum.

m.p. 203 - 204°.

Yield 0.35 g.

$C_{17}H_{13}NO$ requires C 82.6%, H 5.3%, N 5.7%.

$C_{17}H_{11}NO$ requires C 83.3%, H 4.5%, N 5.7%.

found C 83.2%, H 4.5%, N 5.6%.

A dinitrophenylhydrazone of the above compound was prepared by boiling the ketone (0.1 g.) in acetic acid (3 mls.) with dinitrophenylhydrazine hydrochloride (5 mls. stock solution) and conc. hydrochloric acid (2 drops). The addition of sodium bicarbonate solution to this precipitated a crimson solid which was recrystallised several times from acetic acid.

$C_{23}H_{15}N_5O_4$ requires N 16.5%.

found N 16.8%.

Decarboxylation of 1'-hydroxyindeno-2':3'-7:6-quinaldine-4-carboxylic acid by distillation from lime.

The acid (1.0 g.) was intimately mixed with calcium oxide (4.0 g.) by grinding together in a mortar. The mixture was placed in a pyrex tube (9" x $\frac{3}{4}$ "), heated gently at first and then to a dull red heat. A red oil distilled which solidified on cooling. This material was dissolved in benzene and/

and chromatographed on alumina ($2\frac{1}{2}$ " x $\frac{1}{2}$ "). A colourless band, fluorescing brilliantly white in U.V. light, quickly developed and was eluted with benzene. The nearly colourless benzene solution on evaporation deposited colourless needles which were recrystallised from benzene/light petroleum.

m.p. 168 - 169°.

A mixture of this substance and that obtained by decarboxylating indeno-2':3'-7:6-quinaldine-4-carboxylic acid melted at 168 - 170°.

The reduction of 1'-oxoindeno-2':3'-7:6-quinaldine.

The ketone (0.47 g.), obtained by decarboxylating 1'-hydroxyindeno-2':3'-7:6-quinaldine-4-carboxylic acid, was dissolved in trimethylene glycol (25 mls.). Hydrazine hydrate (1 ml., 90%) and sodium hydroxide (0.30 g.) were added to this solution and the whole boiled for 2 hours. The condenser was removed and boiling was continued until the temperature of the mixture reached 200°. Boiling was continued for a further 3 hours. The trimethylene glycol was removed under reduced pressure. Water was added to the residue and this was then extracted with ether (2 x 25 mls.). The ether solution was dried over anhydrous sodium sulphate and then distilled to dryness. The colourless crystalline material remaining was crystallised from aqueous ethanol in colourless needles, m.p. 167 - 168°. This substance on admixture with indeno-2':3'-7:6-quinaldine melted at 167 - 168°.

Yield 0.30 g., 61%.

Oxomalonie ester/

Oxomalonic ester.

This substance was prepared in good yield by the method given in "Organic Synthesis."

Ethyl indeno-2':3'-6:5-dioxindole-3-carboxylate.

This substance was prepared as described by Neish loc. cit., who, however, does not state the yield obtained. It was found that the yield varied for no apparent reason, attempts to isolate further quantities of product or to recover starting material from mother liquors were unsuccessful.

m.p. 246 - 249°, lit. m.p. 249°.

Yield (from 10 g. 2-aminofluorene), 6 - 8 g.,

38 - 50%.

Indeno-2':3'-6:5-isatin.

The method of Neish always involved the formation of a yellow crystalline substance which had to be boiled with hydrochloric acid and acetic acid in order to obtain the isatin.

The above dioxindole (5.0 g.) was dissolved in a mixture of methanol and water (50 mls.) containing potassium hydroxide (3.0 g.). This mixture was heated on a boiling water bath for 2 hours during which time air was bubbled through the solution. Acetic acid was added to the solution until just acid, and then the solution was evaporated to half bulk. The isatin was obtained as an amorphous powder which was recrystallised from acetic acid.

m.p. 247 - 250° d., lit. m.p. 260° d.

Yield 2.51 g., 61%.

2-Aminofluorenone./

2-Aminofluorenone.

2-Nitrofluorenone (10 g.) was suspended in boiling acetone (500 mls.). To this was added sodium sulphide (20 g.) dissolved in the minimum of hot water. After boiling for 2 hours the solution was evaporated to dryness, dissolved in ethanol (charcoal). The solution was reduced to small bulk and set aside to cool. 2-Aminofluorenone was obtained as dark violet plates.

m.p. 158 - 159°, lit. m.p. 160°.

Yield 6.5 g., 76%.

Ring closure of 2-aminofluorenone and oxomalonate ester.

2-Aminofluorenone (5 g.) in acetic acid (80 mls.), was added to oxomalonate ester (5 g.) in acetic acid (80 mls.), and the whole boiled for 2 hours. The solution was then reduced to half bulk and set aside to cool. The material which crystallised out was removed and recrystallised from glacial acetic acid.

decomposes 290 - 300°.

Yield 0.7 g., 9%.

requires C 66.9%, H 4.1%, N 4.3%.

found C 65.8%, H 4.4%, N 4.6%.

Attempted Pfitzinger reaction with 2':3'-6:5-indenoisatin and acetone.

2':3'-6:5-Indenoisatin (2.0 g.), acetone (6 mls.) and potassium hydroxide were dissolved in ethanol (50 mls.) and the solution boiled for 56 hours. The solution changed colour from greenish blue to a deep golden brown during the period of boiling. On acidifying/

acidifying to pH. 6 with acetic acid a brown precipitate appeared which was removed and dried over phosphorus pentoxide in a vacuum dessicator. An attempt was made to esterify this material by boiling in methanol with sulphuric acid. A minute amount of material was obtained which melted 150 - 157°.

Esterification was also attempted by the Fischer-Speier method. A slightly larger quantity of this material was obtained but again could not be completely purified, m.p. 154 - 159°.

This reaction was repeated replacing the acetone with acetoxime (5 g.); no better results were achieved.

Attempted Pfitzinger reaction with 2':3'-6:5-indenoisatin and pyruvic acid.

The reaction was carried out as above with pyruvic acid (4 g.) in place of the acetone. The product melting > 360° was sublimed under vacuum (0.01 m.m. Hg.) and at a temperature of 270°. The sublimate appeared to be ^amixture of partially decarboxylated acids for the analysis approximated more closely to a monocarboxylic acid than to a dicarboxylic acid. This material was not investigated further.

2-Phenylindenocinchoninic acid.

A boiling solution of 2-aminofluorene (3.0 g.) in ethanol (10 mls.) was gradually added to a boiling solution of pyruvic acid (1.1 g.) and benzaldehyde (2.0 g.) in ethanol (25 mls.). The cinchoninic acid precipitated out almost at once. After 1 hour's heating it was collected, washed with ethanol and then/

then ether. Further purification was not attempted.

m.p. 265 - 270°, lit. m.p. 272°.

Yield 3.31 g., 65%.

Decarboxylation of the above acid.

Decarboxylation could be effected either by the quinoline and copper method or by distillation from lime. The latter method gave the better yield. The product was again purified by chromatography and was obtained as colourless needles.

m.p. 222 - 223°.

Yield from 1 g., 0.37 g., 40% theory.

requires C 90.1%, H 5.2%, N 4.8%.

found C 89.6%, H 5.0%, N 5.4%.

Doebner Miller reaction with 2-aminofluorene-indeno-2':3'-7:6-quinaldine.

2-Aminofluorene (2.1 g.) hydrochloric acid (4 mls., conc.), paraldehyde (3.0 g.) and anhydrous zinc chloride (1.5 g.) were warmed together on a water bath. At 70° a vigorous reaction occurred which abated after a few minutes. Heating was continued on the boiling water bath for a further 90 minutes. The dark red oil was poured into water (20 mls.) containing sodium hydroxide (5.0 g.). The aqueous solution was decanted from the black tarry material, which was then washed with water. The black tar was extracted into benzene and the benzene solution washed with water. The solution was dried by distilling down to small bulk, and was then chromatographed on alumina (4" x $\frac{3}{4}$ "). Benzene quickly developed/

developed a colourless band with a brilliant white fluorescence in U.V. light. On elution with benzene and distilling down to small bulk a substance crystallising in needles was obtained. This was recrystallised from benzene/petrol.

m.p. 168° , lit. m.p. $133 - 135^{\circ}$, $145 - 159^{\circ}$.

Yield 0.31 g., 10%.

A mixture of this substance and indeno-2':3'-7:6-quinaldine, obtained by decarboxylating Neish's acid melted at 168° .

Oxidation of indeno-2':3'-7:6-quinaldine to indeno-2':3'-7:6-quinaldehyde.

Indeno-2':3'-7:6-quinaldine (0.5 g.) and selenium dioxide (0.5 g.) were dissolved in dioxan (70 mls.) containing water (5 mls.). The mixture was boiled for 3 hours and selenium was deposited. Charcoal (0.2 g.) was added, the solution boiled for a few more minutes and then filtered hot. The solution was evaporated to half bulk, water added until a permanent precipitate appeared and then set aside to cool. The reddish coloured precipitate was removed and dissolved in boiling ethanol. A small quantity of mercury was added and the solution boiled for 1 hour. Charcoal was added and the boiling continued for a few more minutes when the solution was filtered hot. The alcoholic solution, now quite colourless, was reduced to half bulk and set aside to cool. The aldehyde was obtained as colourless needles.

m.p. $221 - 222^{\circ}$.

Yield 0.21 g., 40%.

$C_{17}H_{11}N O$ requires C 83.3%, H 4.5%, N 5.7%.
 found C 83.2%, H 4.6%, N 5.6%.

Oxidation of indeno-2':3'-7:6-quinaldehyde to
 indeno-2':3'-7:6-quinaldinic acid.

Indeno-2':3'-7:6-quinaldehyde (0.30 g.) was dissolved in the minimum of acetone (200 mls., A.R.), hydrogen peroxide (2 mls., 30%) was added to the mixture and the whole boiled for 3 hours. During this time yellow needles of the acid appeared. The solvent was removed leaving a yellow, crystalline mass which was recrystallised from glacial acetic acid.

m.p. 238 - 239°.

Yield 0.19 g., 57%.

$C_{17}H_{11}N O_2$ requires C 78.2%, H 4.3%, N 5.4%.
 found C 77.7%, H 4.6%, N 5.4%.

Decarboxylation of indeno-2':3'-7:6-quinaldinic acid.

The acid (0.10 g.) was intimately mixed with calcium oxide (0.60 g.). The mixture was heated gently at first and then more strongly, an orange oil distilling out. The oil was dissolved in benzene and chromatographed on alumina (1" x $\frac{1}{4}$ "). A colourless band, fluorescing brilliantly white in U.V. light, developed and was eluted with benzene. A colourless compound crystallising in plates was obtained which melted at 132 - 133°. Mixed with "Diels quinoline" this melted at 132 - 133°. Yield 0.007 g.

β-(2-Fluorenylamino)-propenyl methyl ketone.

Prepared according to the method of Buu-Hoi.

Cyclisation/

Cyclisation of the above Schiffs base -
2:4-dimethylindeno-2':3'-7:6-quinoline.

The ring closure was attempted as described by Buu-Hoi.

The Schiffs base (1.0 g.) was added to cold, conc. sulphuric acid (5 mls.), and then gradually warmed to 80° on a water bath. Pouring into water produced a gelatinous precipitate which was soluble in ammonia. Acidifying with sulphuric acid gave back the precipitate while acidifying with hydrochloric acid gave no precipitate. This is discussed in section 2.

Ring closure was now attempted with polyphosphoric acid. A solution of polyphosphoric acid was made by dissolving phosphorus pentoxide (1.0 g.) in glacial phosphoric acid (10 mls.). To this solution was added the Schiffs base, with stirring. The mixture was heated on a boiling water bath during which time it assumed a deep, golden yellow colour. The solution was poured into water, basified and extracted with ether (2 x 100 mls.). The etherial solution was washed with a little water, dried over anhydrous sodium sulphate and evaporated to dryness. The quinoline was obtained as an oil which solidified immediately on the addition of light petroleum. The crystals were removed and recrystallised from benzene/light petroleum yielding 2:4-dimethylindeno-2':3'-7:6-quinoline as nearly colourless prisms.

m.p. 157 - 158°, lit. m.p. 160°.

Yield 0.72 g., 79%.

4-Hydroxymethylindeno-2':3'-7:6-quinaldine.

Methyl indeno-2':3'-7:6-quinaldine-4-carboxylate (0.50 g.) was dissolved in dry benzene (100 mls., A.R.) and added to a solution of lithium aluminium hydride (0.50 g.) in dry ether (200 mls.). The mixture was boiled for 2 hours after which 200 mls. of solvent were removed. Water (100 mls.) containing caustic soda (1.0 g.) was cautiously added after which the remaining solvent was boiled off. The precipitate in the aqueous layer was removed and dried over phosphorus pentoxide. The carbinol was sublimed, or recrystallised from dichlorobenzene.

m.p. 225 - 227°.

Yield 3.34 g., 71%.

Analysis showed that this substance was not pure, but showed that it was essentially the required compound. It was not found possible to obtain this substance analytically pure.

4-Chloromethylindeno-2':3'-7:6-quinaldine.

The above carbinol (0.20 g.) was dissolved in a mixture of phosphorus oxychloride (3 mls.) and phosphorus trichloride (3 mls.). The solution was boiled for 2 hours and then evaporated to dryness under vacuum. Sodium bicarbonate solution was added to the residue which was then extracted into ether. On removing the ether a resinous material remained from which no crystalline substance could be obtained. The experiment was repeated by boiling a suspension of the carbinol in benzene with phosphorus trichloride. This/

This again resulted in the formation of much resin.

The reaction was not investigated further.

2:4-Dimethylindeno-2':3'-7:6-quinoline.

The above carbinol (1.0 g.) was intimately mixed with zinc dust (5.0 g.). The mixture was heated to a dull red heat when a quantity of red oil distilled out. This oil was dissolved in benzene and chromatographed on alumina (2" x $\frac{3}{8}$ "). Development and elution with benzene gave a colourless solution which on evaporation deposited nearly colourless prisms, which were recrystallised from benzene/light petroleum.

m.p. 158°.

Yield 0.18 g., 20%.

This substance when mixed with the product of Combes synthesis with 2-aminofluorene melted 157 - 158°.

β -(2-Fluorenylamino)-crotonate.

Prepared according to Hughes loc. cit.

4-Hydroxyindeno-2':3'-5:6-(or 7:6)quinaldine.

Prepared according to Hughes loc. cit.

Attempted preparation of 4-chloroindeno-2':3'-5:6-(or 7:6)quinoline.

The hydroxy compound (1.0 g.) was boiled in phosphorus oxychloride (7 mls.) for 2 hours. The mixture was then evaporated to dryness under reduced pressure and the residue treated with sodium bicarbonate solution. This left a resinous material from which no crystalline substance could be obtained. The hydroxy compound (0.5 g.) was boiled with phosphorus trichloride (3 mls.) in benzene suspension. No reaction/

reaction took place due to the sparing solubility of the starting material in the benzene.

Zinc dust distillation of the above hydroxy compound.

The hydroxy (0.50_g) compound was intimately mixed with zinc dust (3.0 g.) and heated. Charring took place at quite a low temperature. No material distilled out of the mixture.

All analyses were by Drs. Weiler and Strauss. Melting points were taken with a Kofler hot stage microscope and are uncorrected.

ABSORPTION SPECTRA

The ultra violet absorption spectra of 1'-oxoindeno-2':3'-7:6-quinoline, 1'-oxoindeno-2':3'-7:6-quinaldine, 1'-oxoindeno-2':3'-5:6-quinoline, indeno-2':3'-7:6-quinaldine and 2-phenylindenoquinoline were measured with a Unicam spectrophotometer. The solvent used in each case was 95% ethanol.

1'-Oxoindeno-2':3'-7:6-quinoline.

<u>λ Max.</u>	<u>Log ϵ</u>	<u>λ Min.</u>	<u>Log ϵ</u>
3780	2.49	3680	2.48
2810	4.81	2280	4.18

1'-Oxoindeno-2':3'-7:6-quinaldine.

<u>λ Max.</u>	<u>Log ϵ</u>	<u>λ Min.</u>	<u>Log ϵ</u>
3790	2.56	374	2.50
3670	2.56	365	2.53
3630	2.61	362	2.57
3220	3.90	318	3.89
3025	4.34	300	4.25
3850	4.80.		

1'-Oxoindeno-2':3'-5:6-quinoline.

<u>λ Max.</u>	<u>Log ϵ</u>	<u>λ Min.</u>	<u>Log ϵ</u>
4250	2.84	3800	2.77
3550	3.56	3500	3.42
3400	3.51	3270	3.30
3250	3.31	3140	3.17
2660	4.72	2370	3.97.

Indeno/

Indeno-2':3'-7:6-quinaldine.

<u>λ Max.</u>	<u>Log ϵ</u>	<u>λ Min.</u>	<u>Log ϵ</u>
3450	4.19	3370	3.97
3290	4.08	3220	3.85
3200	3.98	3180	3.86
3080	4.04	3020	3.97
2950	4.03	2920	4.01
2840	4.14	2820	4.14
2650	4.73	2590	4.67
2560	4.69	237	4.36
2350	4.39	234	4.37

2-Phenylindenquinoline.

<u>λ Max.</u>	<u>Log ϵ</u>	<u>λ Min.</u>	<u>Log ϵ</u>
3700	3.83	3620	3.65
3580	3.74	3480	3.63
3390	3.63	3310	3.56
3240	3.59	3180	3.52
3160	3.53	3010	3.44
2720	4.10	2560	3.86
2540	3.89	2500	3.73
2480	3.79	2450	3.69
2420	3.74	2400	3.69
2280	4.02	2270	3.84

C O N C L U S I O N

A summary of the chemistry of fluorene, relevant to the ring closure reactions studied, has been presented. Experiments leading to the synthesis of 1'-oxoindeno-2':3'-5:6-quinoline have been described. The structure of the "Diels quinoline" has been established, and by removing the substituent groups from the indenoquinaldine of Hughes and the indenoquinaldine-4-carboxylic acid of Neish and comparing the product with the "Diels quinoline," the structure of these two compounds has been established. 2:4-Dimethylindeno-2':3'-7:6-quinoline was synthesised from indeno-2':3'-7:6-quinaldine-4-carboxylic acid and found to be identical with the product of Combe's reaction applied to 2-aminofluorene.

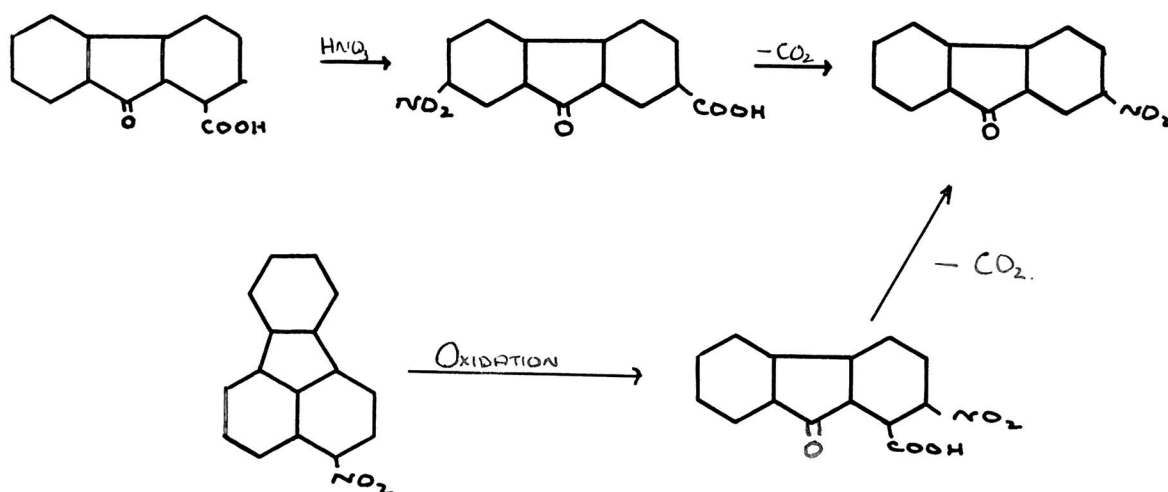
Comparison of the ultra violet absorption curves of 1'-oxoindeno-2':3'-5:6-quinoline and 1'-oxoindeno-2':3'-7:6-quinoline with those of 1:2 and 2:3-benzfluorenone respectively provides additional evidence for the structures assigned to these two quinolines.

It is suggested that the temperature at which cyclisation is carried out is responsible for the direction of ring closure taken by the reaction. Suggestions for further work to establish this as fact, have been made.

NITRATION OF FLUORENE & FLUORENONE-1-CARBOXYLIC ACIDS.

INTRODUCTION

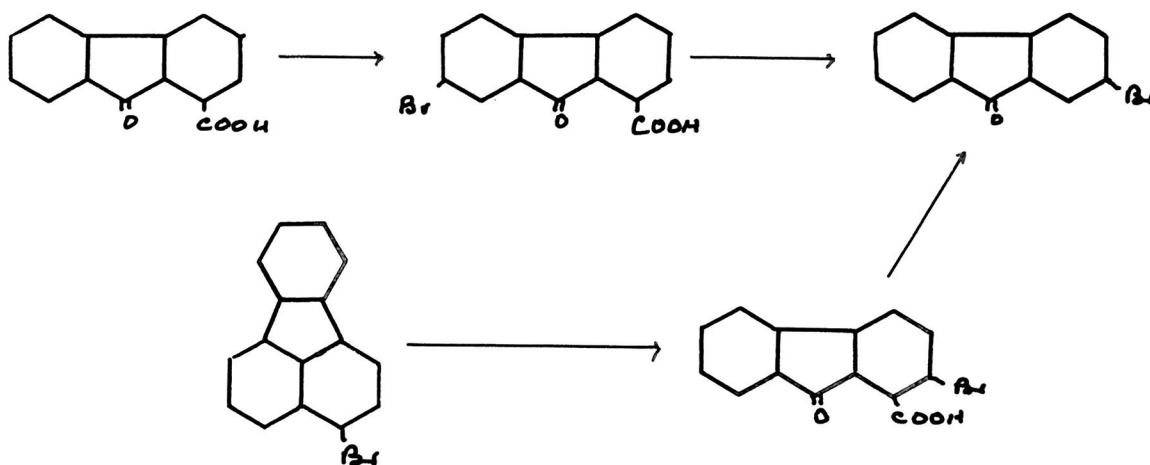
Fittig and Liepman (1) studied the nitration of fluorenone-1-carboxylic acid in 1880 but since then little attention has been paid to this aspect of fluorene chemistry. These workers isolated a nitrofluorenone-1-carboxylic acid which they did not orientate. Seventy years later Fries (2) repeated this work and determined the structure of the acid in the following way. The acid was decarboxylated to 2-nitrofluorenone thus showing the nitro group to be in the 2 or 7 position. 2-Nitrofluorenone-1-carboxylic acid was prepared by the oxidation of 4-nitrofluoranthene and was not identical with the product of nitration of fluorenone-1-carboxylic acid. This acid must, therefore, be 7-nitrofluorenone-1-carboxylic acid.



Campbell and Stafford (3) investigating methods for the preparation of 1:2 substituted fluorenes or fluorenones nitrated fluorenone-1-carboxylic acid and obtained a dinitrofluorenone-1-carboxylic acid, which/

which they did not orientate.

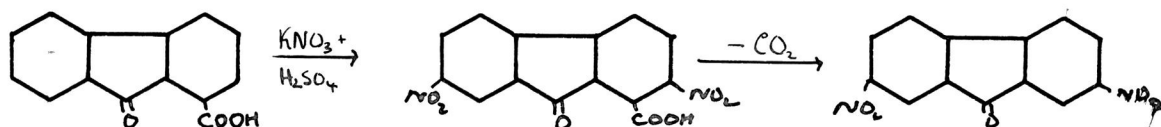
The only other published work on the substitution reactions of this acid is that of Campbell and Rayment (4). 7-Bromofluorenone-1-carboxylic acid was required as a reference compound for the orientation of bromofluoranthenes. This substance was prepared by the direct bromination of fluorenone-1-carboxylic acid and its structure proven in the following way. The acid was decarboxylated to 2-bromofluorenone thus showing the bromine atom to occupy either position 2, or 7. 2-Bromofluorenone-1-carboxylic acid was synthesised by the oxidation of 4-bromofluoranthene and was found not to be identical to the product of bromination of fluorenone-1-carboxylic acid. The structure of this acid must, therefore, be 7-bromo-fluorenone-1-carboxylic acid.



The object of this work was to determine the structure of the dinitrofluorenone-1-carboxylic acid of Campbell and Stafford and to study the nitration of fluorene-1-carboxylic acid.

DISCUSSION

Fluorenone-1-carboxylic acid obtained by the oxidation of fluoranthene (5) was nitrated in the way described by Campbell and Stafford (3) giving a dinitrofluorenone-1-carboxylic acid. This acid was easily decarboxylated with quinoline and copper, the ease of decarboxylation suggesting that one of the nitro groups was adjacent to the carboxyl. The product was easily purified by chromatography followed by crystallisation and was found to be identical to authentic 2:7-dinitrofluorenone. 2:7-Dinitrofluorenone was prepared by nitrating fluorene (6), separating the mixture of isomers by fractional crystallisation and then oxidising the 2:7-dinitrofluorene with chromic oxide. The acid must, therefore, be 2:7-dinitrofluorenone-1-carboxylic acid.



Having orientated the dinitrofluorenone-1-carboxylic acid, the nitration of fluorene-1-carboxylic acid was undertaken. Fluorene-1-carboxylic acid was prepared in good yield by the Wolff Kishner reduction of fluorenone-1-carboxylic acid (7).

Potassium nitrate was added to a solution of this acid in conc. sulphuric acid, on pouring into water very little precipitate appeared, much sulphonation apparently/

apparently having taken place. Other methods of nitration were tried. The acid was dissolved in nitric acid (d. 1.42) and the solution warmed on a water bath. The reaction product was recrystallised many times from alcohol or acetic acid yielding a small amount of a dinitrofluorene-1-carboxylic acid. The mother liquors from the recrystallisation were worked up for any other isomer which might be present but no pure compound could be isolated. An attempt to decarboxylate this acid was made using the conventional quinoline and copper method. A very small amount of a very high melting material was obtained in yield insufficient for analysis. Because of the wasteful and difficult purification procedure required in isolating the acid, the investigation was abandoned at this stage.

The nitration of fluorene-1-carboxylic acid with nitric acid (d. 1.5) was now studied. By dissolving in nitric acid and heating at 100° for 1 hour a trinitrofluorene-1-carboxylic acid was obtained which could be purified by recrystallisation, from glacial acetic acid. Decarboxylation of this acid was attempted several times under different reaction conditions, but no neutral compound could be isolated from the reaction product. Since difficulty had been encountered with the dinitrofluorene-1-carboxylic acid in this reaction, it was decided to oxidise the trinitro acid to the fluorenone and then attempt the decarboxylation. Several experiments were undertaken to find the best conditions for the oxidation. Boiling the/

the acid in glacial acetic acid with chromic oxide or sodium dichromate gave very low yields of the ketone. The best method was found to be by boiling a suspension of the acid in dilute sulphuric acid with sodium dichromate. The decarboxylation of this trinitrofluorenone-1-carboxylic acid was attempted with quinoline and copper, but again it was found impossible to isolate any pure compound from the reaction product.

It was thought that the above acid might be obtained by the nitration of 2:7-dinitrofluorenone-1-carboxylic acid; this was attempted but it was found that the 2:7-dinitrofluorenone-1-carboxylic acid could not be nitrated even by boiling with a mixture of fuming nitric acid and conc. sulphuric acid.

EXPERIMENTALFluorenone-1-carboxylic acid.

Fluoranthene (10 g.) was boiled with sodium dichromate (150 g.) in glacial acetic acid for 18 hours. The solution was distilled down to half bulk and poured into dilute sulphuric acid (700 mls., 30%). The precipitate was filtered off, washed with a little dilute sulphuric acid and then with water until free of acid. The fluorenone-1-carboxylic acid could be recrystallised from glacial acetic acid as orange needles.

m.p. 194° , lit. m.p. 194° .

Yield 7.2 g., 65% theory.

Dinitrofluorenone-1-carboxylic acid.

Fluorenone-1-carboxylic acid (1.0 g.) was dissolved in conc. sulphuric acid (5 ml.). Potassium nitrate (1 g.) was added over a period of 5 minutes. The resulting solution was warmed to 80° on a water bath for 1 hour and then poured into ice-water (100 g.). The yellow solid was recrystallised from glacial acetic acid yielding yellow plates.

m.p. 264° , lit. m.p. 264° .

Yield 0.8 g., 59%.

Decarboxylation of above acid.

The acid (0.3 g.) was heated in quinoline (5 mls.) at 180° with copper bronze (0.01 g.); at this temperature CO_2 was freely evolved. After 15 minutes the solution was poured into dil. hydrochloric acid, (20 mls.) and the precipitate removed. The precipitate was/

was dissolved in benzene and chromatographed on alumina. A pale yellow band developed and was eluted with benzene. On evaporation to small bulk the solution deposited fine yellow needles which were recrystallised from glacial acetic acid.

m.p. 192°

292°?

Yield (0.01 g.), 38%.

2:5 and 2:7 Dinitrofluorene.

Fluorene (10 g.) was added to a mixture of glacial acetic acid (50 mls.) and fuming nitric acid (50 mls.), and allowed to stand at room temperature for 15 minutes. The yellow precipitate obtained by pouring the mixture into water was filtered off and dried. This material was extracted 3 times with 25 ml. portions of acetic acid. The residue was then recrystallised from glacial acetic acid yielding pale yellow needles, decomposing at 269° . 2:5-Dinitrofluorene was recovered from the acid extracts.

2:7-Dinitrofluorenone.

2:7-Dinitrofluorene (1.0 g.) was dissolved in the minimum of boiling acetic acid, chromic oxide (1.0 g.) was added to the solution in 4 lots over a period of 15 minutes. The solution was boiled for $1\frac{1}{2}$ hours. The reaction mixture was chilled, greenish yellow needles being deposited. This material was recrystallised from glacial acetic acid giving yellow needles, m.p. $190 - 191^{\circ}$, lit. $190 - 191^{\circ}$. Mixed m.p. of the substance obtained by the decarboxylation of the dinitrofluorenone-1-carboxylic acid with the above authentic 2:7-dinitrofluorenone showed no depression.

292°?

Fluorene/

Fluorene-1-carboxylic acid.

Fluorenone-1-carboxylic acid (3.2 g.), sodium hydroxide (2 g.), hydrazine hydrate (2 ml., 85%) and trimethylene glycol (27 mls.) were refluxed together for 3 hours. The condenser was removed and the mixture allowed to boil until the temperature of the solution reached 205°. Refluxing was continued for a further 2½ hours. On pouring into dilute hydrochloric acid a white precipitate was obtained which was recrystallised from glacial acetic acid.

m.p. 242 - 243°, lit. m.p. 243°.

Yield 2.5 g., 83%.

Dinitration of fluorene-1-carboxylic acid.

Fluorene-1-carboxylic acid (1.0 g.) was added in small portions to nitric acid (30 mls., d. 1.42); the solution was heated for 2 hours on a boiling water bath. A yellow precipitate formed after 10 minutes heating, this slowly redissolved so that after a further 30 minutes a clear yellow solution remained. On pouring into water a yellow precipitate was thrown down which was filtered off and well washed with water. This material was recrystallised from alcohol repeatedly giving a pale yellow substance which sublimed at 250 - 260° and melted 279 - 281°. Yield 35 mgm.

The experiment was repeated. The crude product was taken up in the minimum of boiling alcohol and the solution allowed to stand for 2 hours. The solid which crystallised out was removed and recrystallised from glacial acetic acid yielding needles, m.p. 281 - 283°. Yield/

Yield 84 mgm.

$C_{14}H_1N_2O_6$ requires N 9.3%.

found N 10%.

No pure compound could be isolated from the alcoholic mother liquors from the above.

Decarboxylation of above acid.

The acid (20 mgm.) was dissolved in quinoline (2 mls.) and a pinch of copper bronze powder added. Carbon dioxide was evolved at 180 - 200°, heating was continued at this temperature for 30 minutes. The mixture was poured into dilute hydrochloric acid and extracted with benzene. The benzene extract was dried, reduced to small bulk and chromatographed on alumina (3" x $\frac{1}{4}$ "). A yellow band developed and was eluted with benzene. Small pale yellow needles were obtained, m.p. >360° in quantity insufficient for analysis

Trinitration of fluorene-1-carboxylic acid.

Fluorene-1-carboxylic acid (0.5 g.) was added to nitric acid (5 mls., d. 1.5) and the solution heated on a boiling water bath for 1 hour. The solution was poured into ice-water (20 g.) and the precipitate removed and washed well with water. Recrystallisation twice from glacial acetic acid yielded pale yellow needles, m.p. 256 - 257°. Yield 0.5 g., 60%.

$C_{14}H_7N_3O_8$ requires C 48.7%, H 2%, N 12.2%.

found C 48.9%, H 2.1%, N 11.8%.

Attempted decarboxylation of trinitrofluorene-1-carboxylic acid.

The/

The above acid (0.1 g.) was dissolved in quinoline (5 mls.) containing copper bronze (0.01 g.). The mixture was heated for 1 hour at 220 - 230°. The quinoline was steam distilled off, and the residue extracted with benzene. No neutral substance was obtained from this solution.

This reaction was repeated replacing the quinoline with pyridine. The acid (0.1 g.) was dissolved in pyridine (7.5 mls.) containing copper bronze (0.01 g.). The mixture was boiled for 1 hour after which it was poured into dilute acid. The aqueous solution was extracted with benzene which was back extracted with carbonate, dried and reduced to small volume. The solution was chromatographed on alumina; a pale yellow band appeared which was eluted with benzene. This solution yielded pale yellow crystals in very small amount on evaporation to dryness. No pure substance was obtained.

The experiment was repeated reducing the period of boiling to 30 minutes, again no pure substance could be isolated.

Oxidation of trinitrofluorenone-1-carboxylic acid.

The acid (1.0 g.) and sodium dichromate (25 g.) were boiled together in dilute sulphuric acid (165 mls., 10%) for 4½ hours. The reaction mixture was cooled, the solid removed and recrystallised several times from alcohol. The keto acid crystallised in golden yellow plates, m.p. 249 - 260°. This m.p. could not be/

be improved.

Yield 0.25 g., 24%.

$C_{14}H_5N_3O_9$ requires N 11.7%.

found N 11.9%.

Attempted decarboxylation of trinitrofluorenone-1-carboxylic acid.

The acid (0.01 g.) was dissolved in quinoline (5 ml.) and copper bronze (0.01 g.) added. The solution was heated to 180° and kept at this temperature for 1 hour. The quinoline was removed by steam distillation and the residue extracted into benzene. The benzene solution was dried and chromatographed on alumina. A pale yellow band developed which was eluted with benzene. On removal of the solvent a small amount of a buff coloured substance was obtained which could not be purified.

Attempted nitration of 2:7-dinitrofluorenone-1-carboxylic acid.

The acid (1.0 g.) was added to a mixture of nitric acid (10 mls., d. 1.5) and sulphuric acid (10 mls.) and boiled for 4 hours. Starting material was returned almost quantitatively.

CONCLUSION

The dinitrofluorenone-1-carboxylic acid obtained by Campbell and Stafford was found to be 2:7-dinitrofluorenone-1-carboxylic acid. The nitration of fluorene-1-carboxylic acid gave according to the conditions a mixture of dinitrofluorene-1-carboxylic acids of which one was isolated in pure form, or a trinitrofluorene-1-carboxylic acid. These acids could not be decarboxylated satisfactorily, the investigation was therefore abandoned at that point.

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POSTSCRIPT

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ABSTRACT OF THESIS

Name of Candidate ARTHUR F. TEMPLE.
Degree Ph.D. Date October 1954.
Title of Thesis Ring Closures in the Fluorene Series.

Diels, in 1902, applied the Skraup procedure to 2-amino-fluorene and isolated one indenoquinoline, which must be indeno - 2':3'-5:6 - quinoline or indeno - 2':3' - 7:6 - quinoline. This substance was not orientated. Since then a number of workers have synthesised py - substituted Quinolines from 2-aminofluorene, but in only one case has the structure of the quinoline been determined. The object of this work was to determine the structure of the "Diels quinoline" and other substituted quinolines derived from 2-aminofluorene.

A review of the chemistry of fluorene relevant to the ring closure reactions studied, is presented.

The orientation of the "Diels quinoline" was attempted by degradation. The attempted unambiguous synthesis of indeno-2':3' - 5:6 - quinoline from 3 - nitro - 2 - aminofluorene and 3:7 - dibromo - 2 - aminofluorene and indeno - 2':3' - 7:6 - quinoline from 4 - aminofluoranthene and 6 - nitro - 7 - methyl-quinoline, are described. 1' - oxoindeno - 2':3' - 5:6 - quinoline was successfully synthesised from 3 - azachrysene and shown not to be identical to the product of oxidation of the "Diels quinoline", which must, therefore, be indeno - 2':3' - 7:6 - quinoline.

An unsuccessful attempt to synthesise indeno - 2':3' - 7:6 - quinaldine - 4 - carboxylic acid from indeno - 2':3' - 6:5 - isatin is described. By removing the substituent groups from the product of the Doebner Miller and Doebner pyruvic acid synthesis on 2-aminofluorene, these were shown to be indeno-2':3' - 7:6 - quinaldine and indeno - 2':3' - 7:6 - quinaldine - 4 - carboxylic acid/

acid respectively.

2:4 - dimethylindeno - 2':3' - 7:6 - quinaldine was synthesised from indeno - 2':3' - 7:6 - quinaldine - 4 - carboxylic acid and shown to be identical to the product of the Combes synthesis applied to 2 - aminofluorene.

A comparison of the U.V. absorption curves of 1' - oxoindeno - 2':3' - 5:6 - quinoline and 1' - oxoindeno - 2':3' - 7:6 - quinoline with 1:2- and 2:3- benzfluorenone respectively provides additional evidence for the structures assigned to the two quinolines.

It is suggested that the temperature at which cyclisation of derivatives of 2-aminofluorene is carried out is responsible for the direction taken by the reaction. Suggestions for further work are made.

A short section at the end of the thesis is devoted to the substitution reactions of fluorenone - 1-carboxylic acid. A dinitrofluorenone - 1 - carboxylic acid first prepared by Campbell and Stafford was shown to be 2:7 - dinitrofluorenone - 1 - carboxylic acid. The nitration of fluorene - 1 - carboxylic acid was also studied.

RING CLOSURES OF 2-AMINOFLUORENE

REACTION	PRODUCT	POINT OF RING CLOSURE
<u>2-Aminofluorene</u>		
Skraup's synthesis	Indeno-2':3'-7:6-quinoline	3
Doebner - Miller reaction	Indeno-2':3'-7:6-quinaldine	3
Doebner's pyruvic acid synthesis	Indeno-2':3'-7:6-quinaldine-4-carboxylic acid	3
Doebner's pyruvic acid synthesis with benzaldehyde	2-Phenylindenoquinoline-4-carboxylic acid	Not known
" " " " " piperonal	2-Piperonylindenoquinoline-4-carboxylic acid	"
" " " " " anisaldehyde	2-Anisylindenoquinoline-4-carboxylic acid	"
Combe's synthesis	2:4-Dimethylindeno-2':3'-7:6-quinoline	3
Conrad Limpach reaction	4-Hydroxyindenoquinaldine	1
Knorr's reaction	2-Methylindenocarbostyryl	Not known
Martinet's reaction	3-Carbethoxyindeno-2':3'-6:5-dioxindole	" ?
Treatment with ethoxymethylenemalonie ester	3-Carbethoxyindeno-2':3'-5:6-carbostyryl	" ?
<u>2-Aminofluorenone</u>		
Skraup's synthesis	1'-Oxoindeno-2':3'-7:6-quinoline	3
Doebner's pyruvic acid synthesis with benzaldehyde	1'-Oxo-2-phenylindenoquinoline-4-carboxylic acid	Not known
" " " " " piperonal	1'-Oxo-2-piperonylindenoquinoline-4-carboxylic acid	"
Combe's synthesis	1'-Oxo-2:4-dimethylindenoquinoline	"